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1 **On the origin of the difference between type A and type B**
2 **skeletal isomerization of alkenes catalyzed by zeolites:**
3 **the crucial input of ab initio molecular dynamics**

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13

14 **ABSTRACT**

15 Alkene skeletal isomerisation elementary steps catalyzed by acid zeolites are key reactions in
16 refining, petrochemistry and biomass conversion. We unravel the atomic-scale origin of the
17 higher rate constant of type A isomerization (involving a direct alkyl transfer, without any
18 change in the branching degree) than the one of type B isomerization (involving non-classical
19 carbonium ions such as protonated cyclopropane (PCP), inducing a change in the branching
20 degree) of C_7 carbenium ions in chabazite. Accurate free energy barriers are calculated at 300
21 and 500 K for both reactions by means of molecular dynamics in combination with blue
22 moon ensemble approach, whereas the static approach is shown to fail to describe these
23 reactions. The slow transformation between individual rotational isomers, causing non-
24 ergodic sampling of reactant state, largely overlooked in literature, is carefully addressed in
25 the present work. At 500 K (representative of experimental conditions), free energy barriers
26 of 83.4 kJ/mol and 15.0 kJ/mol are determined for type B and type A isomerization
27 respectively. The much lower barrier for type A is thus recovered, and assigned to a loose
28 transition state, with free rotation of the migrating alkyl group, while the transition state of
29 type B isomerization is tighter, with such a rotation blocked, due to the simultaneous hydride
30 shift taking place on the edge of the PCP.

31

32 **KEYWORDS:** carbenium; protonated cyclopropane; blue moon ensemble; chabazite;
33 rotamers.

34 1. INTRODUCTION

35 Carbenium chemistry is at the core of a large set of chemical transformations in
36 organic chemistry [1–6], with crucial current and prospective industrial repercussions. As a
37 major example, the bi-functional isomerization of alkyl chains is a key reaction in refining
38 [7,8], petrochemistry [8,9] and biomass conversion [10–12]. Hydrocracking and
39 hydroisomerization are among the major industrial current processes based on carbenium
40 chemistry. They are utilized for instance in production of diesel and jet fuels from
41 conventional fossil resources [13], in technologies making use of the heaviest parts of
42 hydrocarbons obtained via the Fischer-Tropsch process from different feedstock (coal,
43 biomass or gas), or for very heavy unconventional crudes such as tar sands and shale oils
44 [14,15]. Hydrocracking and hydroisomerization catalysts typically combine two functions: a
45 hydrogenation/dehydrogenation function on a noble metal or a metallic sulfide and an acidic
46 function of the Brønsted type provided by zeolites or amorphous silica-aluminas [15].

47 A sequence of reactions taking place in these processes begins by the dehydrogenation
48 of alkanes into alkenes. The alkenes are protonated afterwards on the acidic function.
49 Intermediate carbocations are formed and these species evolve by isomerization and β -
50 scission reactions. The resulting shorter and isomerized alkenes are hydrogenated to form
51 alkanes, which are eventually desorbed as products [15,16]. The isomerization reactions of
52 alkenes are typically catalyzed by acid zeolites at temperatures around 250 °C and at a partial
53 pressure of H₂ of around 1-10 bars [15,16].

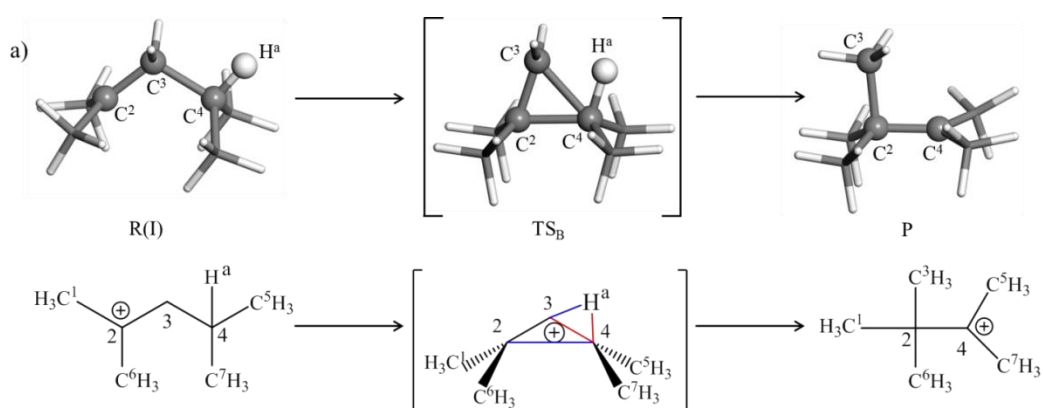
54 The isomerization is classified as type A when it does not lead to any branching
55 degree change (in practice, this corresponds to a direct hydride or 1,n alkyl transfer [17]), or
56 type B when an increase in the branching degree of the chain occurs. These transformations
57 involve non-classical carbonium ions such as protonated cyclopropane (PCP) [8,17–19]. The
58 latter are often invoked for type B isomerization but are also likely to be relevant in the case

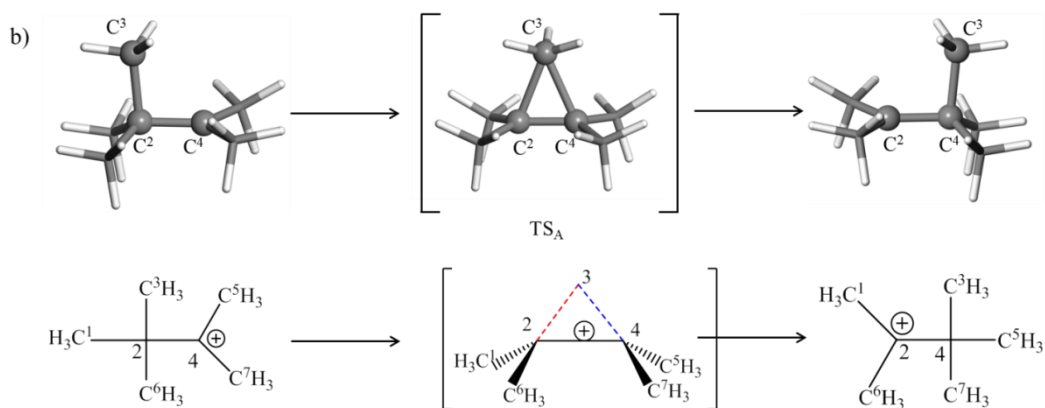
59 of type A alkyl-shifts. Type B isomerization reactions are of interest when cracking is aimed
60 at, as higher branching degree is expected to allow the preferential formation of tertiary or
61 secondary carbenium ions (instead of primary ones) favoring easier cracking [8,20]. It is
62 known that type A isomerization is several orders of magnitude faster than type B
63 isomerization [8,15–17,21]. However, the molecular origin of such a ranking is still poorly
64 understood. Moreover, the intermediate *versus* transition state nature of the PCP is debated
65 for a long time [22]. Earlier static *ab initio* calculations dealing with zeolites suggest that it
66 should be a transition state [23–28], but the determination of the energy profile was biased by
67 the alkoxide nature of the reactants and products, whereas more recent *ab initio* molecular
68 dynamics showed that, at finite temperature, tertiary carbenium ions exist in significant
69 concentrations [29,30]. Finally, determining accurately the intrinsic free energy barrier for
70 type A and type B isomerization reactions is rather challenging, as the isomerization reactions
71 generally occur simultaneously, and together with hydrogenation-dehydrogenation reactions,
72 plus cracking. Single-event kinetic schemes were successful in fitting experimental data in
73 that respect, and also in reproducing the expected trend according to which type A is faster
74 than type B [31–35]. However, considering the number of adjustable parameters in these
75 models, quantifying the intrinsic free energy barriers for these elementary steps by an
76 independent approach is called for.

77 Herein, we report a density functional theory (DFT) investigation addressing these issues.
78 We analyze the free energetics of type B isomerization connecting a C₇ dibranched tertiary
79 cation (2,4-dimethyl-pent-2-enium cation) to a tribranched tertiary cation (2,3,3-trimethyl-
80 but-2-enium cation) and we compare the free energy barriers with those of type A
81 isomerization involving the same tribranched tertiary cation (Figure 1). The model reactions
82 studied herein are the “building blocks” for the key elementary steps of the
83 hydroisomerization of alkanes, in practice however, the rate constants of these individual

84 steps are not easy to quantify. Lumping of steps is usually performed in single-event kinetic
 85 modeling approach, which prevents a detailed mechanistic analysis. As a model for the
 86 catalyst, the acid chabazite zeolite is considered in this work. In the literature, the finite
 87 temperature effects are most often introduced via static approach to the transition state theory
 88 (TST) consisting of atomic relaxations followed by calculations of harmonic vibrational
 89 frequencies, which are subsequently employed in approximate formulae for free energy,
 90 enthalpy, and other thermodynamic quantities of interest. Previous theoretical work [36–38],
 91 however, demonstrated that such a simple approach can not provide satisfactory results for
 92 free energy analysis of hydrocarbon conversions in zeolites. Free energy methods based on
 93 molecular dynamics (MD) [29,30,36–46] or Monte Carlo (MC) simulations [47,48], which
 94 are designed to study chemical reactions, are free of limitations of the static approach. Due to
 95 their high computational cost and a non-trivial realization, the use of these methods in
 96 theoretical catalysis is still rather limited. To the best of our knowledge, they were never used
 97 for the type A versus type B isomerization of alkenes.

98





100

101 **Figure 1.** Isomerization reactions: a) type B between 2,4-dimethyl-pent-2-enium cation and 2,3,3-
 102 trimethyl-but-2-enium cation, b) type A between two symmetry equivalent 2,3,3-trimethyl-but-2-
 103 enium cations. Note that the reactant of reaction b) is identical with the product of reaction a). The
 104 ball and sticks structures are optimized in gas phase. The blue and red lines indicate the bonds that
 105 are, respectively, formed and broken during the reactions.

106 We investigate these mechanisms with advanced *ab initio* molecular dynamics
 107 methods (blue moon ensemble approach), that we compare with a more traditional static
 108 approach. The uncertainty of the latter is estimated by an ensemble of converged simulations
 109 describing a large set of stationary points. The treatment of interconversions between
 110 rotational isomers, that is largely overlooked in simulations in the literature, appeared to be
 111 key for the accurate determination of pathways and free energies: we propose here a rigorous
 112 treatment of this problem. We then reach, with aid of *ab initio* molecular dynamics, a
 113 quantification of the intrinsic free energy barriers and an atomistic explanation of the
 114 difference between type A and type B isomerization kinetics.

115

116 2. METHODOLOGY

117 2.1 Total energy calculations

118 Periodic DFT calculations were performed using the VASP code [49,50]. The Kohn-
 119 Sham equations have been solved variationally in a plane-wave basis set using the projector

120 augmented-wave (PAW) method of Blöchl [51], as adapted by Kresse and Joubert [52]. The
121 PBE exchange-correlation functional in the generalized gradient approximation proposed by
122 Perdew et al. [53] was used. The D2 correction of Grimme [54] has been applied to account
123 for long-range dispersion interactions that are not treated correctly by local and semilocal
124 density-functional theory. Despite its simplicity, this approach has been shown [55] to
125 improve predictions on structure, energetics, and elastic properties of wide range of materials
126 where dispersion forces play an important role. The PBE+D2 method was also shown to
127 predict reasonable adsorption energies for some of the zeolite-related applications [56]. As a
128 relatively large supercell was employed in calculations (*vide infra*), the Brillouin zone
129 sampling was restricted to the Γ -point. A plane-wave cutoff energy of 400 eV was used in all
130 calculations and the convergence criterion for the electronic self-consistency cycle was set to
131 10^{-7} eV. In the simulations of cations in the gas phase, the charge neutrality of the simulation
132 cell has been preserved by using a compensating uniform background charge.

133 **2.2 Transition state search through the static approach**

134 In order to ensure that the reactant, transition state, and product configurations
135 obtained in atomic relaxations discussed in Sections 3.1 and 3.2 are linked by same reaction
136 coordinate, the following strategy has been applied. In the first step, the first-order saddle
137 point on the potential-energy surface corresponding to the transition state for the reaction of
138 interest was identified using the improved dimer method [57,58]. Subsequently, the intrinsic
139 reaction coordinate [59,60] (IRC) for the forward and backward reaction steps was identified
140 using the damped velocity Verlet algorithm [61]. Next, the terminal points from the IRC
141 calculations were relaxed using a conjugate-gradient algorithm [62]. In all atomic relaxations
142 of minima and saddle points, the structures were considered as relaxed when all forces acting
143 on the atoms were smaller than 0.005 eV/Å. Finally, the vibrational eigenspectrum of relaxed
144 structures has been examined and additional line-minimization calculations along undesired

145 unstable modes have been performed until the computed eigenspectrum contained a correct
 146 number of imaginary vibrational frequencies (i.e. zero for stable structures and one for
 147 transition states). All relaxations with fixed internal coordinates and a part of the TS
 148 optimizations have been performed using the optimization engine GADGET [63,64].

149 **2.3 Molecular dynamics simulations**

150 Born Oppenheimer molecular dynamics simulations (MD) have been performed in the
 151 (NVT) ensemble. The temperature was controlled with the Andersen thermostat [65] with a
 152 collision frequency per atom of 0.01 fs^{-1} . The classical equations of motion were integrated
 153 using the leapfrog algorithm with an integration step of 1 fs. The atomic mass of tritium has
 154 been chosen for all H atoms in order to avoid possible numerical instabilities due to the use of
 155 a relatively large integration step. Free energies have been computed using the simulation
 156 protocol described in Ref. [43] In this approach based on the transition state theory [65,66],
 157 the free-energy of activation (ΔA^\ddagger) is defined as follows:

$$\Delta A^\ddagger = \Delta A_{\xi_{ref,R} \rightarrow \xi^*} - k_B T \ln \left(\frac{h}{k_B T} \frac{\langle |\dot{\xi}^*| \rangle}{2} P(\xi_{ref,R}) g_R \right), \quad (1)$$

158 where $\Delta A_{\xi_{ref,R} \rightarrow \xi^*}$ is the reversible work needed to shift the value of reaction coordinate (ξ)
 159 from some arbitrary reference value characteristic for reactant ($\xi_{ref,R}$) to the value ξ^*
 160 defining the free-energy transition state, $\langle |\dot{\xi}^*| \rangle$ is the average absolute value of velocity of
 161 reaction coordinate at the transition state, $P(\xi_{ref,R}) = \langle \delta(\xi - \xi_{ref,R}) \rangle_R$ is the probability
 162 density of the state $\xi_{ref,R}$ in ensemble of all reactant (R) configurations, and g_R is the number
 163 of symmetry equivalent choices of $\xi_{ref,R}$ corresponding each to a different stable isomer of
 164 reactant. As in Ref. [43], the term $\Delta A_{\xi_{ref,R} \rightarrow \xi^*}$ is obtained from the blue moon ensemble
 165 method (BM) [67,68] implemented in VASP [69], $P(\xi_{ref,R})$ is determined using the
 166 straightforward MD simulations, and $\langle |\dot{\xi}^*| \rangle$ is computed numerically using a constrained MD
 167 with $\xi(r) = \xi^*$. Free energies of reaction ($\Delta A_{R \rightarrow P}$) are computed similarly:

$$\Delta A_{R \rightarrow P} = \Delta A_{\xi_{ref,R} \rightarrow \xi_{ref,P}} - k_B T \ln \left(\frac{g_R P(\xi_{ref,R})}{g_P P(\xi_{ref,P})} \right). \quad (2)$$

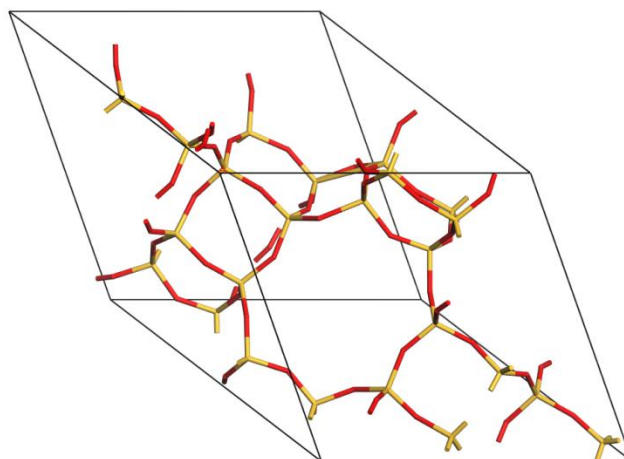
168 In Equation (2), $\Delta A_{\xi_{ref,R} \rightarrow \xi_{ref,P}}$ is the reversible work needed to shift the value ξ from
 169 $\xi_{ref,R}$ to some arbitrary reference value $\xi_{ref,P}$ characteristic for product (P), $P(\xi_{ref,P})$ is the
 170 probability density of the state $\xi_{ref,P}$ which is, similarly to $P(\xi_{ref,R})$, determined using
 171 straightforward MD of the product state, and g_P is the number of symmetry equivalent
 172 choices of $\xi_{ref,P}$ corresponding each to a different stable isomer of product. We emphasize
 173 that the free energies computed using Equations 1 and 2 are independent of the particular
 174 choice of the approximation to the reaction coordinate, provided the approximation drives the
 175 transformation from reactant to product reversibly. This property is particularly important
 176 when comparing the free energetics of chemical reactions differing in reaction mechanisms
 177 and consequently also in definitions of ξ . Our method is very closely related to the Bennett-
 178 Chandler approach, which is by design invariant with the CV choice [43,65,66]. One can see
 179 from equations 1 and 2 or related rate and equilibrium constants expressions [43,65] that all
 180 these quantities have correct dimensions independent of the CV choice.

181 Details of calculations of individual terms of Equations 1 and 2 as well as the
 182 corresponding numerical values are presented in Sections SI and SII. The length of
 183 straightforward MD simulations used to determine probability densities of reference states
 184 was at least 100 ps (see Table S.1) while the length of all constrained MD runs performed
 185 with the BM simulations was 50 ps. In each MD run, the initial period of 5 ps has been
 186 considered as equilibration and the corresponding data were not used in calculations of
 187 ensemble averages. Undesired by-reactions, such as the deprotonation of the reactant or
 188 product molecules, have been prevented by the use of restraining potentials described in
 189 Section SIII.

190 A slow growth simulation protocol [70] (MD in which a candidate CV is increased at a
191 constant rate) has been employed in a qualitative way to make sure that the candidate CV can
192 indeed drive smoothly the reaction of interest – from the reactant to the product state, as
193 illustrated in Supporting Information SIV. Our choice of the approximation of reaction
194 coordinate (CV) was validated in a number of internal tests (Supporting Information SIV).

195 **2.4 Structural Model**

196 A primitive rhombohedral cell of purely siliceous chabazite (CHA framework,
197 symmetry group $R\bar{3}m$), with 12 symmetry equivalent tetrahedral sites, was obtained from
198 International Zeolite Association (IZA) database [71]. The cell was optimized (with a cutoff
199 energy of 800 eV) and the resulting lattice constants $a = 9.336 \text{ \AA}$ and $\alpha = 94.6^\circ$ are found to
200 be in a good agreement with the experimental reference values [71] ($a = 9.304 \text{ \AA}$ and $\alpha =$
201 94.6°). The relaxed structure was subsequently used to build a supercell defined by the lattice
202 vectors \mathbf{a}'_1 , \mathbf{a}'_2 , and \mathbf{a}'_3 related to the primitive cell vectors of rhombohedral lattice ($\mathbf{a}_1, \mathbf{a}_2, \mathbf{a}_3$)
203 via the following transformations: $\mathbf{a}'_1 = \mathbf{a}_2 + \mathbf{a}_3$, $\mathbf{a}'_2 = \mathbf{a}_1 + \mathbf{a}_3$, and $\mathbf{a}'_3 = \mathbf{a}_1 + \mathbf{a}_2$ (Figure 2).
204 The shortest interatomic separation between the atoms in hydrocarbon and the atoms in its
205 periodically repeated images was not shorter than 5.5 \AA . We note that for the sake of
206 consistency, the same supercell has been used also in the gas phase simulations. One of the Si
207 atoms (which are all symmetry equivalent) has been substituted by an Al atom introducing
208 thus a negative charge into the zeolite framework. This negative charge can be formally
209 compensated by attaching a proton onto a framework oxygen atom creating thus a Brønsted
210 acid site (BAS). In this work, however, we investigate reactions in which cationic molecular
211 species occur at all stages whereby the positive charge of cations originates from the proton
212 transferred from the BAS to a neutral molecule. For this reason, no particular Brønsted acid
213 site needs to be considered.



214

215 **Figure 2.** Supercell of chabazite used in simulations. (Si in yellow and O in red).

216 **3. RESULTS AND DISCUSSION**

217 **3.1. Isomerization mechanisms and question of the reactant / product rotamers: static** 218 **approach applied to gas phase reactions**

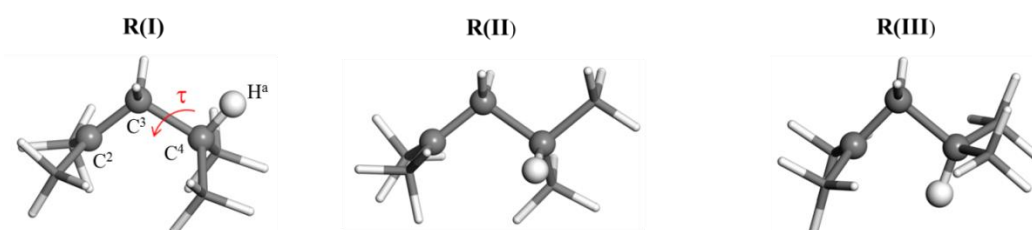
219 We start by analyzing isomerization reactions of type B and A occurring in the gas
220 phase, which represents the simplest realization of both reactions. The results presented here
221 will be used as reference data for more complicated reactions occurring in zeolite (Sections
222 3.2, 3.3 and 3.4). Note that all stationary states have been obtained using unconstrained
223 relaxations with very stringent relaxation criteria. A particular attention has been paid to
224 ensure correctness of corresponding eigenvalue spectra. Thus all the stationary states
225 representing reactants and products are all correct unconstrained potential energy minima.

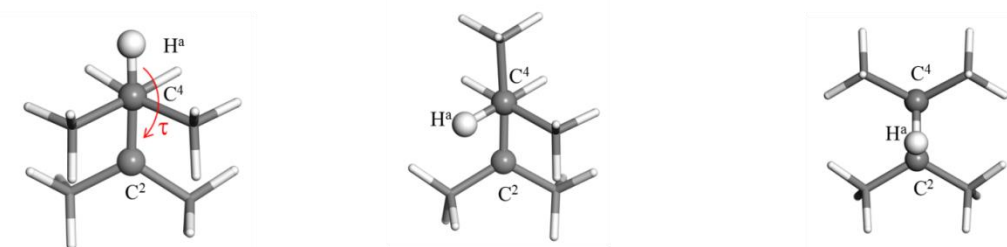
226 The reactant molecule for type B isomerization (2,4-dimethyl-pent-2-enium cation)
227 forms four stable rotational isomers (rotamers) that can be distinguished by measuring the
228 torsional angle $H^a-C^4-C^3-C^2$ (τ): R(I) with $\tau = 180$ deg., R(III) with $\tau = 0$ deg., and two
229 symmetry equivalent rotamers R(II) with $\tau = \pm 59.1$ deg. The structure of stable rotamers
230 and the numbering of atoms are shown in Figure 3. Potential energy as a function of τ
231 obtained in a series of constrained relaxations is shown in Figure 4. As evident, the most

232 stable rotamer R(II) is 3.4 kJ/mol and 1.1 kJ/mol lower in potential energy compared to the
 233 cations R(I) and R(III), respectively. Importantly, however, only the conformation of rotamer
 234 R(I) is such that type B isomerization is sterically allowed (see below). Indeed, the hydrogen
 235 atom H^a is transferred from C⁴ to C³, while the C²-C⁴ bond is formed and the C³-C⁴ bond is
 236 broken in the course of this reaction (Figure 1 and Figure 3). Hence the first step of reaction
 237 is a transformation of a generic reactant molecule being in any of its stable rotational isomers
 238 into the rotamer R(I). As shown in Figure 4, the potential energy barriers for the
 239 transformations R(II) → R(I) and R(II) → R(III) (18.7 kJ/mol and 4.6 kJ/mol, respectively) are
 240 relatively small compared to the reaction barrier for type B isomerization (*vide infra*). It is
 241 therefore reasonable to expect that all rotamers are always at equilibrium with one another
 242 and the probability to find the state R(I) at the fixed temperature, volume, and number of
 243 particles (NVT ensemble) is given by the Boltzmann distribution law:

$$p(R(I)) = \frac{e^{-A(R(I))/k_B T}}{e^{-A(R(I))/k_B T} + 2e^{-A(R(II))/k_B T} + e^{-A(R(III))/k_B T}} \quad (3)$$

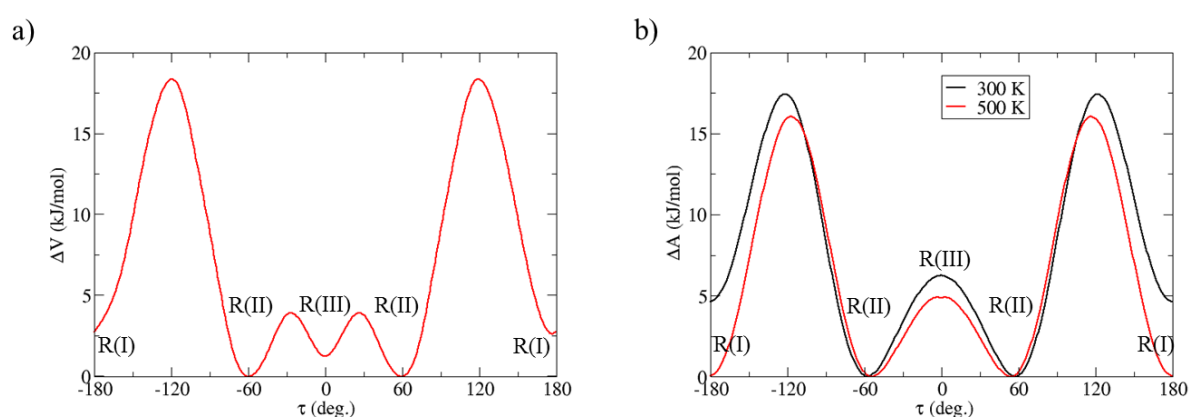
244 where $A(i)$ is the Helmholtz free energy of the state i and the factor 2 in the denominator
 245 reflects the two-fold degeneracy of the state $R(II)$. Using the usual harmonic oscillator and
 246 rigid rotor approximation (hereafter termed as static approach), we obtained the values of 4.6
 247 % and 7.5 % for the term $p(R(I))$ at T=300 K and 500 K, respectively. As discussed below,
 248 the term $p(R(I))$ contributes to the free energy of activation.





250

251 **Figure 3.** Rotational isomers R(I) ($\tau = 180$ deg.), R(II) ($|\tau| = 59.1$ deg) and R(III) ($\tau = 0$ deg.) of the
 252 reactant 2,4-dimethyl-pent-2-enium cation. Top panel: side view; bottom panels: front view chosen so
 253 that the atom C4 overlaps the atom C3.



254

255 **Figure 4.** a) Potential energy profile along dihedral angle τ computed for the 2,4-dimethyl-pent-2-
 256 enium cation in the gas phase at $T=0$ K, and b) free energy profile computed using MD for the same
 257 molecule in chabazite at 300 K and 500 K.

258

259 The transition state for type B isomerization (TS_B) in the gas phase was identified by
 260 the static approach and its structure is shown in Figure 1-a. TS_B is an edge-protonated PCP.
 261 In TS_B , the two pairs of methyl groups connected to C^2 and C^4 are face-to-face. By the IRC
 262 approach (see movie in supporting information), we show that TS_B is connected to the R(I)
 263 rotamer, in which these methyl groups are in the same conformation. Starting from another
 264 rotamer (Figure 3) necessary needs to rotate first to generate R(I) then TS_B that are
 265 connected. The computed electronic activation energy $\Delta A_{eL,R(I) \rightarrow TS_B}$ equals 70.4 kJ/mol. The

266 free-energy barrier for type B isomerization in the gas phase defined with respect to a generic
267 reactant state R, consisting of all rotational isomers distributed according to the Boltzmann
268 law, can be computed using the formula:

$$\Delta A_{R \rightarrow TS_B} = \Delta A_{R(I) \rightarrow TS_B} - k_B T \ln(p(R(I))g_{R(I)}), \quad (4)$$

269 where the term $\Delta A_{R(I) \rightarrow TS_B} = A(TS_B) - A(R(I))$, which we designate hereafter as the
270 microprocess barrier, corresponds to the free energy of activation for the reaction starting
271 from the active rotamer R(I), whereas the last term on the right hand side is the correction
272 reflecting the fact that the state R(I) is only one of four possible reactant states. As the state
273 R(I) is non-degenerate, the degeneracy factor $g_{R(I)}$ equals unity. The free energy barrier
274 computed using the static approach $\Delta A_{R \rightarrow TS_B}$ increases with temperature as follows: 84.5
275 kJ/mol (300 K), and 93.4 kJ/mol (500 K). Similarly, the microprocess barriers ($\Delta A_{R(I) \rightarrow TS_B}$)
276 computed for T=300 K, and 500 K are 76.8 kJ/mol, and 82.7 kJ/mol, respectively (see Figure
277 6). Clearly, the correction term $-k_B T \ln(p(R(I)))$ is always positive leading to an increase of
278 free-energy barrier. Furthermore, its contribution (of the order of 10 kJ/mol) increases with
279 increasing temperature, which is obvious from the explicit presence of T in this term (the
280 much weaker implicit dependence introduced via equation (3) tends to decrease $\Delta A_{R(I) \rightarrow TS_B}$
281 with increasing T). As shown by Tables S2 and S3, the rise of the microprocess barrier with
282 T is mainly due to the entropic term $-T\Delta S_{R(I) \rightarrow TS_B}$ (in particular its vibrational component),
283 which increases by 7.6 kJ/mol when T is changed from 300 K to 500 K, whereas the internal
284 energy of activation changes only by -1.6 kJ/mol at the same temperature interval. The
285 relatively large negative vibrational entropy of activation follows from the loose reactant and
286 tight transition state picture: compared to the reactant, two new bonds (C^2-C^4 and C^3-H^a) are
287 being formed while the bonds C^3-C^4 and C^4-H^a present also in the reactant are not yet
288 completely broken in TS_B , and hence the PCP transition state structure is geometrically more
289 constrained than the structure of reactant (Figure 1).

290 The reaction product, the 2,3,3-trimethyl-but-2-enium cation, forms six symmetry
291 equivalent rotational isomers (see Figure S12) separated by a potential energy barrier of 3.0
292 kJ/mol. The free-energy of reaction R→P writes:

$$\Delta A_{R \rightarrow P} = \Delta A_{R(I) \rightarrow P(i)} - k_B T \ln \left(\frac{p(R(I))g_{R(I)}}{p(P(i))g_{P(i)}} \right). \quad (5)$$

293 Similar to Equation (4), the term $\Delta A_{R(I) \rightarrow P(i)} = A(P(i)) - A(R(I))$ is the free energy
294 difference between the particular product and reactant configurations $P(i)$ and $R(I)$, whereas
295 the last term accounts for the fact that these states are formed with a certain likelihood among
296 all possible product and reactant configurations. We note that the contributions of $p(P(i))$
297 and $g_{P(i)}$ to Equation 5 cancel each other because all rotational isomers of the product states
298 are symmetry equivalent and hence $p(P(i)) = \frac{1}{g_{P(i)}}$. The computed potential energy for the
299 product cation is 4.4 kJ/mol lower than that of the configuration R(I) and the term $\Delta A_{R(I) \rightarrow P(i)}$
300 varies with T as follows: -4.9 kJ/mol (300 K), and -5.0 kJ/mol (500 K). The sign and
301 magnitude of $\Delta A_{R(I) \rightarrow P(i)}$ are almost fully determined by the internal energy of reaction
302 (Table S3), whereas the entropy of reaction is negligible (the computed values of
303 $-T\Delta S_{R(I) \rightarrow P(i)}$ are 0.0 kJ/mol at 300 K and 0.6 kJ/mol at 500 K). Taking the configurational
304 term $-k_B T \ln(p(R(I)))$ into account, both the sign and the value of $\Delta A_{R \rightarrow P}$ change (2.8
305 kJ/mol (300 K) and 5.8 kJ/mol (500 K)).

306 The product of type B isomerization can further undergo type A isomerization
307 reaction. The product of the latter reaction is, in the case considered in this work, chemically
308 identical to the reactant (i.e. 2,3,3-trimethyl-but-2-enium cation), hence the free energy,
309 internal energy, and entropy of reaction are zero by definition. Unlike type B isomerization,
310 the free energy barrier $\Delta A_{P(i) \rightarrow TS_A}$ depends weakly on T (see Table S4), the computed values
311 are 14.7 kJ/mol (300 K), and 16.2 kJ/mol (500 K) (see Figure 6). In this case, the effect of
312 newly formed bond C³-C⁴ in transition state (TS_A) is compensated by a significant weakening

313 of the C²-C³ bond, which is elongated to the same length as the newly formed C³-C⁴ (1.84 Å).
314 TS_A is a corner-protonated PCP. Hence the structure of the PCP ring in TSA is not more
315 strongly constrained than the reactant configuration and the tight reactant and loose transition
316 state picture valid for type B isomerization does not apply to type A isomerization. This result
317 explains why the computed entropy of activation takes a relatively small value (the computed
318 values of $-T\Delta S_{P(i)\rightarrow TS_A}$ are 1.8 kJ/mol and 4.7 kJ/mol for T=300 K and 500 K, respectively).
319 As all rotamers formed by the reactant (or product) molecule are equivalent by symmetry, the
320 last term in the formula $\Delta A_{P\rightarrow TS_A} = \Delta A_{P(i)\rightarrow TS_A} - k_B T \ln(p(P(i))g_{P(i)})$ is zero due to
321 cancellation of terms $p(P(i))$ and $g_{P(i)}$ and hence the free energy of activation is identical to
322 the microprocess free energy barrier.

323

324 **3.2. Static approach applied to reactions in zeolite**

325 Within a zeolite framework, the mechanisms of both isomerization reactions remain the
326 same as in the gas-phase because the atoms of the zeolite framework are not covalently
327 bonded to the intermediates involved. Nevertheless, the electrostatic interaction and
328 dispersion forces between the zeolite and the molecule increase tremendously the complexity
329 of the potential energy surface (PES), which now contains many local stationary points
330 corresponding to structures differing in the orientation and the relative position of the
331 molecule with respect to the zeolite internal surface at each step of the reaction. In this
332 section, we demonstrate that the increased complexity of PES introduces an unacceptably
333 large and hard to control error into the calculations of reaction free-energetics determined via
334 the static approach.

335 To this end, a set of seven TS configurations has been determined by means of geometric
336 relaxations for both chemical reactions considered in this work, whereby the initial
337 configurations (used for the relaxations) have been obtained from constrained molecular

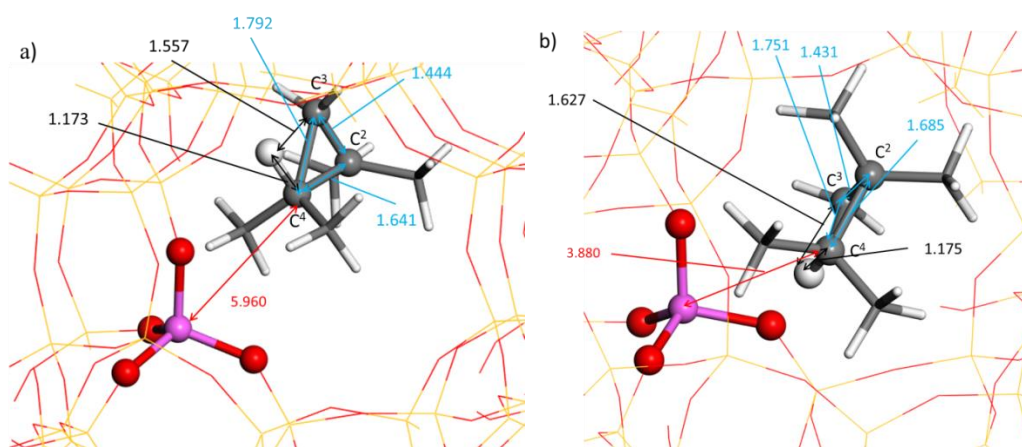
338 dynamics simulations described in Sections 3.3.3 and 3.4.3. In all cases, TS_A and TS_B remain
339 corner and edge-protonated PCPs respectively (see also later, a detailed structural analysis in
340 sections 3.3.4 and 3.4.4.). We emphasize that our sets of TS configurations are by no means
341 exhaustive – they have been chosen only to highlight the strong limitation of the static
342 approach applied to such complex systems. Upon determining the TS configurations, the
343 reactant and product configurations have been obtained by means of the IRC analysis (see
344 Section 2). The vibrational spectra of all relaxed configurations were carefully checked to
345 ensure that all relaxed structures were correct stationary points of PES.

346 As shown in Table S5, the potential energies of optimized TS structures for type B
347 isomerization are spread over a very broad range of values, the difference between the
348 highest and the lowest TS energies being as large as 40.2 kJ/mol. This large variation in
349 energy is due to significant differences in the TS orientation and position within the zeolite
350 framework whereas the molecular structure of each TS is rather similar (Table S8). As shown
351 in Figure S13, the potential energy of individual TS configurations correlates rather well with
352 the parameter χ defined as

$$\chi = \sum_{i=1}^{N_C} \frac{1}{[d(\text{Al} - \text{C}^i)]^6} \quad (6)$$

353 where $d(\text{Al} - \text{C}^i)$ is the distance between aluminum atom and the carbon atom i , and the
354 sum is over all carbon atoms in the system (N_C). Taking into account that the framework Al is
355 surrounded by four oxygen atoms with increased negative charge and some of the C atoms
356 bears a partial positive charge, we deduce that the variation of the potential energy of
357 individual TS configurations is mainly attributed to the electrostatic and dispersion
358 interactions between the PCP and the zeolitic framework. The distance C⁴–Al in relaxed TS
359 structures, for instance, varies from 3.88 Å to 5.96 Å (the two extreme cases are shown in
360 Figure 5 while all TS structures are shown in Figure S14 and the corresponding data are

361 given in Table S8) indicating that the PCP can be stabilized in many different places of the
362 zeolite micropores.



363

364

365 **Figure 5.** Selected transition state configurations for type B isomerization: relaxed structure with the
366 longest (a) and the shortest (b) separation between atoms C^4 and Al. (Al in purple, H in white, Si in
367 yellow and O in red). Selected interatomic distances are in Å.

368

369 The variation of vibrational contribution to free energy of TS_B resulting from differences in
370 the low-frequency part of the vibrational spectra (Table S5) are as large as 13.6 kJ/mol (300
371 K) and 22.6 kJ/mol (500 K). The variation in the total free energy of TS_B configurations is
372 ~ 40 kJ/mol for both temperatures considered in this work (Table S5), which is very similar to
373 the variation in the potential energy reported above.

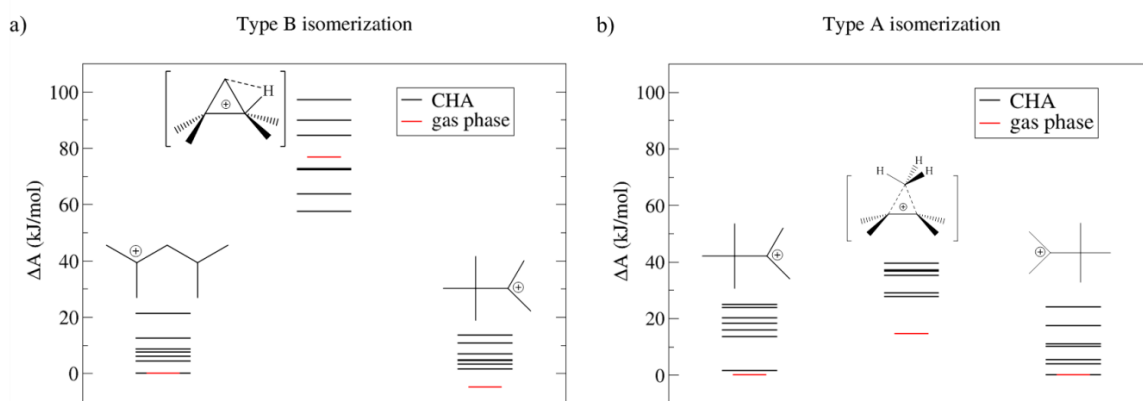
374 Results obtained for type A isomerization (Table S11) show that the variation of potential
375 energy for the relaxed TS_A structures spreads over a narrower interval of width of 11.1
376 kJ/mol (Table S9). As in the case of TS_B , the electronic energy of the TS_A structures
377 identified in this work correlates rather well with the parameter χ defined above (see Figure
378 S13), albeit the spread of the χ values is much narrower. The latter fact indicates that the
379 variation of orientations and positions of TS_A sampled in our static calculations is much
380 smaller than that for the TS_B configurations. The maximal and minimal vibrational free-

381 energy determined for the TS structures at 300 K and 500 K differ by 13.3 kJ/mol and 20.7
382 kJ/mol, respectively. The resulting variation in the total free energy of TS_A is 11.8 kJ/mol and
383 17.4 kJ/mol for $T=300$ K and 500 K, respectively. Once again, the intramolecular structures
384 of all relaxed reactant and product configurations are found to be rather similar to their gas-
385 phase counterparts (see Figure S15 for the first two configurations and the Table S12 with
386 geometric data of the PCPs) and the variation in the computed potential energy stems almost
387 exclusively from the differences in the position and orientation of the molecule in the zeolite.

388 All these results have important practical consequence: if only a single static calculation is
389 performed to explore a chemical reaction similar to those studied in this work, as it is often
390 the case in the literature, the uncertainty in the computed free energy of TS_A is of order of 10
391 kJ/mol (40 kJ/mol for TS_B) and it increases with T .

392 In practice, however, one is usually interested in relative (e.g. free energies of reaction and
393 activation) rather than in absolute free energies of a given state. Hence the important question
394 is to which extent the above-mentioned uncertainty is reflected into the uncertainty in
395 computed free-energy barriers. In order to address it, the reactant and product configurations
396 linked with the different TS configurations have been determined by means of IRC analysis.
397 The contributions to the total free energies are reported in Tables S7 and S11, and illustrated
398 in Figure 6 for type B and type A isomerization reactions at $T=300$ K. The uncertainty in
399 computed free energy differences is enormous.

400



401
 402 **Figure 6.** Distribution of free energy values computed in seven independent simulations based on
 403 static approach for the microprocess transformation of a) type B and b) type A isomerization
 404 reactions in chabazite at $T = 300\text{ K}$. For both reactions, the lowest energy of reactant states defines zero on the
 405 free energy scale. For the sake of comparison, the values computed for the reactions in gas phase are
 406 also shown.

407
 408 Depending on the transition state, the microprocess barrier $\Delta A_{R(I) \rightarrow TS_B}$ for the forward
 409 mode of type B isomerization ranges between 50.1 kJ/mol to 84.5 kJ/mol at 300 K (76.8
 410 kJ/mol in gas phase, Figure 6) and between 52.5 kJ/mol to 85.7 kJ/mol at 500 K (82.7 kJ/mol
 411 in gas phase), respectively (Table S7). The variation in the microprocess barrier for the
 412 reverse mode is similar: 46.8 kJ/mol to 92.6 kJ/mol at 300 K (81.7 kJ/mol in gas phase) and
 413 49.5 kJ/mol to 94.0 kJ/mol at 500 K (87.7 kJ/mol in gas phase). The microprocess barrier for
 414 type A isomerization varies between 8.7 kJ/mol to 37.2 kJ/mol at 300 K and 5.1 kJ/mol to
 415 42.6 kJ/mol at 500 K, respectively (Table S11). As mentioned in Section 3.1, the reactant and
 416 product states of type A isomerization studied in this work are chemically identical, and
 417 hence the forward and reverse reaction modes are indistinguishable.

418 Finally, we point out that the uncertainty in free energy of activation increases further if
 419 one does not ensure that all stationary states of reaction are linked by a common IRC, as it is

420 unfortunately often the case in the literature. On basis of our results we estimate that in the
 421 most extreme case, the microprocess barrier for the forward reaction mode of type B
 422 isomerization at 300 K, for instance, can spread over the interval between 36.4 kJ/mol to 97.2
 423 kJ/mol if the reactant and TS configurations are determined in two independent static
 424 calculations.

425 Altogether, we have shown that the use of the static approach to study isomerization
 426 reactions in zeolites is highly problematic. Clearly, in order to overcome the limitations of
 427 this approach, one has to efficiently sample the configuration space relevant for the reaction
 428 of interest. As we shall discuss in Sections 3.3 and 3.4, this task can be elegantly
 429 accomplished by means of molecular dynamics.

430

431 **3.3. Molecular Dynamics of type B isomerization in zeolite**

432 **3.3.1. Choice of the approximation to the reaction coordinate**

433 The MD method used in this study to determine the free energy of activation (Section 2.3)
 434 requires the use of a suitable approximation of the reaction coordinate (ξ), which must be
 435 able to reversibly drive the reaction from its initial to the final state. For this purpose, we used
 436 a path-based collective variable (ξ) introduced by Branduardi et al. [72], which is defined as
 437 follows:

$$\xi = \frac{1}{M-1} \frac{\sum_{i=1}^M (i-1) \exp(-\lambda |\mathbf{q} - \tilde{\mathbf{q}}(i)|^2)}{\sum_{i=1}^M \exp(-\lambda |\mathbf{q} - \tilde{\mathbf{q}}(i)|^2)}, \quad (7)$$

438 where \mathbf{q} is a multidimensional vector whose components are primitive coordinates
 439 describing the changes in the structure of the system during the reaction, $\tilde{\mathbf{q}}(i)$ is the position
 440 vector (defined in the same primitive coordinate space as \mathbf{q}) of the i -th point of a discretized
 441 reaction path $\{\tilde{\mathbf{q}}(i); i = 1, \dots, M\}$, M is the total number of points in $\{\tilde{\mathbf{q}}(i)\}$, and λ is an
 442 adjustable parameter. The neighboring points of $\{\tilde{\mathbf{q}}(i)\}$ should be approximately equidistant

443 and the parameter λ should be chosen so as to correspond to the average value of $|\tilde{q}(i) -$
444 $\tilde{q}(i + 1)|^2$ [72,73]. By construction, the value of ξ ranges between 0 (reactant) and 1
445 (product).

446 As shown in Sections 3.1 and 3.2, the activation energy of type A isomerization is
447 relatively small and hence this reaction can occur spontaneously during the MD simulations
448 of the product configurations of type B isomerization. In order to prevent this undesired
449 process, the coordinate ξ has been defined so as to cover both subsequent isomerization
450 reactions. To this end, the following lengths of the carbon-carbon and carbon-hydrogen bonds
451 involved in type B and A isomerization reactions have been chosen as the primitive
452 coordinates defining \tilde{q} and q : C^2-C^3 , C^3-C^4 , C^2-C^4 , C^4-H^a , and C^3-H^a (Figure 3). We note that
453 this choice has been made with type B isomerization in mind and it is not optimal for type A
454 isomerization where the atom H^a plays no special role. The reaction coordinates for both
455 reactions have been approximated by the corresponding IRC determined for the gas-phase
456 reaction discussed in Section 3.1 and merged via the common point corresponding to the
457 product of type B isomerization, which is identical to the reactant of type A isomerization
458 (see Section 3.1). The discretized reaction path $\{\tilde{q}(i)\}$ has been subsequently defined by
459 choosing 20 approximately equidistant points. With this setting, the interval of ξ between 0
460 and ~ 0.77 corresponds to type B isomerization while the interval between ~ 0.77 and 1 covers
461 type A isomerization.

462 **3.3.2. Characterization of reactant and product states**

463 As discussed in Section 3.1, out of four rotational isomers of the reactant molecule (2,4-
464 dimethyl-pent-2-enium cation), only the rotamer designated as R(I) can be directly
465 transformed into the transition state for type B isomerization. It is therefore natural to choose
466 a high-likelihood state of the rotamer R(I) as a reference state ($\xi_{ref,R}$) for the use in the free
467 energy calculations (Equation 1). A direct calculation of the probability density $P(\xi_{ref,R})$ by

468 the straightforward MD would be extremely inefficient due to the relatively high free energy
 469 barriers (as compared to $k_B T$) separating the stable rotational isomers of reactant (Figure 4).
 470 In order to circumvent this problem, we express the density of the reference reactant state as
 471 follows:

$$P(\xi_{ref,R}) = \tilde{P}(\xi_{ref,R}) \times p(R(I)), \quad (8)$$

472 where $\tilde{P}(\xi_{ref,R}) = \langle \delta(\xi - \xi_{ref,R}) \rangle_{R(I)}$ is the probability density of the reference state in the
 473 ensemble of all realizations of the state $R(I)$, and $p(R(I)) = \frac{\int_{q \in R(I)} dq dp e^{-\frac{H(q,p)}{k_B T}}}{\int_{q \in R} dq dp e^{-\frac{H(q,p)}{k_B T}}}$ is the
 474 probability of the state $R(I)$ among all reactants states. The two terms of Equation 8 are
 475 computed in two different sets of simulations that we discuss below.

476 The term $p(R(I))$ is obtained from the free energy profile $A(\tau)$ computed using the blue
 477 moon ensemble method [67,68] whereby the torsional angle τ is defined in Section 3.1.
 478 Altogether 10 integration points evenly distributed over the interval $0 \leq \tau < \pi$ have been
 479 used and the full profile $A(\tau)$ ($-\pi \leq \tau < \pi$) has been built by employing the symmetry of the
 480 molecule dictating the relations $A(-\tau) = A(\tau) = A(\tau + 2\pi)$. As obvious from Figure 4, the
 481 finite temperature free energy profiles determined for reactant in chabazite are similar in
 482 shape to the zero temperature potential energy profile computed for the reactant in the gas
 483 phase. The only qualitative difference is the absence of the shallow minimum at $\tau=0$. As we
 484 show in Section SV.1, this interesting variation is caused by the fact that, unlike the isomers
 485 $R(I)$ and $R(II)$, the rotamer $R(III)$ ($\tau=0$) is stable only if the skeletal angle $C4-C3-C2$ (α) is
 486 below 100 deg. At increased temperature, however, the thermal motion of atoms leads to an
 487 increase in average value of α making the isomer $R(III)$ unstable. Apart from this detail, the
 488 calculations predicted the expected trends: an increase in temperature leads to a decrease in
 489 free energy differences between minima corresponding to the stable rotamers $R(I)$ and $R(II)$,
 490 and the barrier for the $R(II) \rightarrow R(I)$ transformation (transition states positioned at $\tau_{max,1} \approx$

491 -120° and $\tau_{max,2} \approx 120^\circ$) decreases with increasing T. The probability of the state R(I)

492 among all reactant configurations, computed using the formula $p(R(I)) = \frac{\int_{\tau_{max,1}}^{\tau_{max,2}} \exp\left(-\frac{A(\tau)}{k_B T}\right) d\tau}{\int_{-\pi}^{\pi} \exp\left(-\frac{A(\tau)}{k_B T}\right) d\tau}$,

493 therefore increases from 6.4 % at T=300 K to 27.9 % at 500 K. We note that while the former
494 value is similar to that determined using the static approach for the cation in gas phase (4.6
495 %), the latter is significantly greater than its static approach gas phase counterpart (7.5 %).

496 Probability density $\tilde{P}(\xi_{ref,R})$ is determined using the straightforward MD of the state R(I).
497 For both simulation temperatures considered in this work, the free energy barriers separating
498 the rotamers R(I) and R(II) are relatively high compared to the $k_B T$ term, which ensures that
499 the transformation R(I)→ R(II) is a slow process occurring only very infrequently on the time
500 scale of our MD simulations. The probability densities computed for T=300 K and 500 K are
501 shown in Section SI. The values determined for the reference state $\xi_{ref,R} = 0.069$ are 23.5
502 (300 K) and 16.3 (500 K). Finally, we determine the following values of $P(\xi_{ref,R})$ using
503 equation 8: 1.5 (300 K) and 4.5 (500 K).

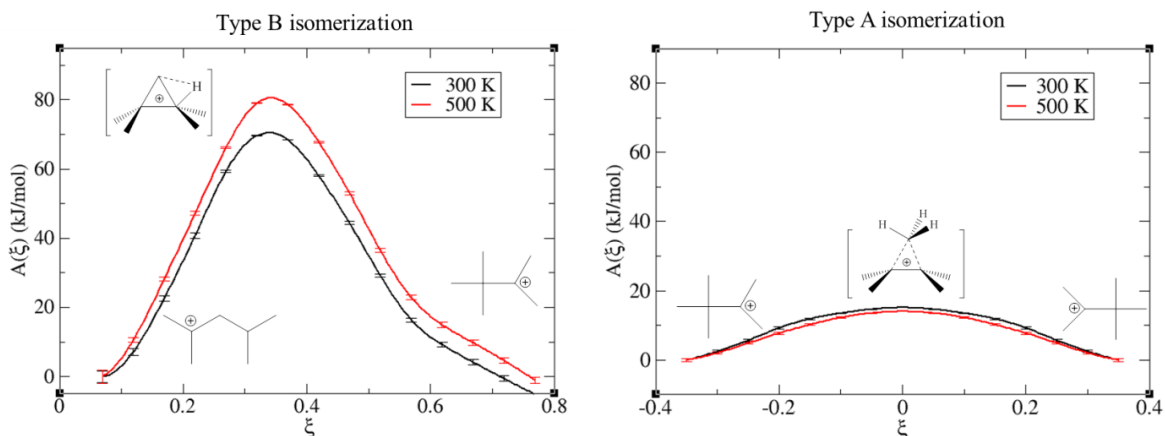
504 A similar analysis has been performed also for the product state (2,3,3-trimethyl-but-2-
505 enium cation formed in chabazite). In this case, the calculation was simplified by the fact that
506 all six stable rotational isomers of the product state are equivalent by symmetry (see Section
507 3.1), and hence the following equality holds: $g_P P(\xi_{ref,P}) = \langle \delta(\xi - \xi_{ref,P}) \rangle_{P(i)}$. Choosing
508 the reference state $\xi_{ref,P} = 0.769$, the calculations based on the straightforward MD
509 performed for the product state led to the following values of $g_P P(\xi_{ref,P})$: 17.9 (300 K) and
510 14.9 (500 K).

511

512 3.3.3. Free energy calculations

513 In order to determine the terms $\Delta A_{\xi_{ref,R} \rightarrow \xi^*}$ and $\Delta A_{\xi_{ref,R} \rightarrow \xi_{ref,P}}$ used in calculations of free
514 energies of activation and reaction (see Section 2.3), blue moon ensemble approach [67,68]

515 has been employed. To this end a mesh of 16 integration points has been used corresponding
516 to states distributed between the reference reactant ($\xi_{ref,R}$) and product ($\xi_{ref,P}$) states defined
517 in Section 3.3.2. The free energy profiles $A(\xi)$ computed for T=300 K and 500 K are shown
518 in Figure 7. The free energy transition state ($\xi^* \approx 0.338$) has been identified as the
519 maximum on $A(\xi)$ and the values of the velocity term $|\dot{\xi}^*|$ ($1.75 \cdot 10^{12} \text{ s}^{-1}$ and $2.29 \cdot 10^{12} \text{ s}^{-1}$
520 for T=300 K and 500 K, respectively) have been determined as described in Section SII. The
521 computed contributions of the term $\Delta A_{\xi_{ref,R} \rightarrow \xi^*} = A(\xi^*) - A(\xi_{ref,R})$ to the free energies of
522 activation at 300 K and 500 K are 70.5 (± 3.4) kJ/mol and 80.5 (± 3.6) kJ/mol, respectively
523 (taking into account the standard error on the mean values of the gradients of the free energy,
524 for a confidence interval of 95%). Employing equation 1 along with the data presented in
525 Section 3.3.2, the free energies of activation of 74.4 (± 3.4) kJ/mol and 83.4 (± 3.6) kJ/mol
526 have been obtained for T=300 K and 500 K, respectively. These values are ~ 10 kJ/mol lower
527 than those computed using the simple static approach for the reaction in the gas phase
528 discussed in Section 3.2. Such a difference is not unexpected as the latter simulations use a
529 more approximate physical model and completely neglect the interactions between the
530 molecule and zeolite. In this light it is remarkable that both sets of simulations predict almost
531 the same change in the free energy of activation (~ 9 kJ/mol) due to the increase of T from
532 300 K to 500 K. This result suggests that the temperature trend in activation energy of this
533 monomolecular reaction is entirely determined by entropy related to the intramolecular
534 vibrations while the contribution of those degrees of freedom related to interactions with
535 zeolite is negligible. This conclusion is even underlined by the similarity in average geometry
536 of transition states identified in MD with the zero temperature TS geometry for the gas phase
537 reaction (see Section 3.3.4), which is consistent with the tight TS and loose reactant picture.



538

539 **Figure 7.** Free energy profiles ($A(\xi)$) computed using the bluemoon ensemble approach for type B
 540 (left) and type A (right) isomerization reactions in chabazite at $T=300$ K and 500 K. The error bars are
 541 determined from the standard errors on the free energy gradients [69].

542

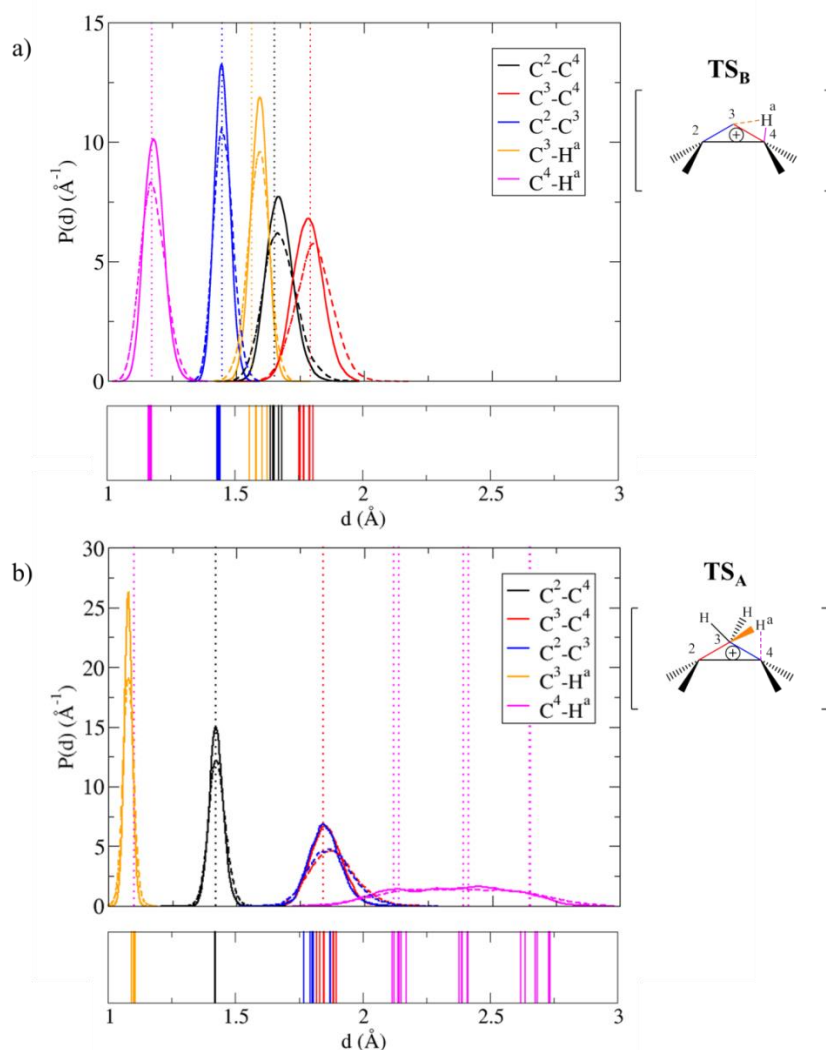
543 The free energies of reaction computed using Equation (2) for $T=300$ K and 500 K are 1.9
 544 (± 3.8) kJ/mol and 3.7 (± 4.2) kJ/mol, respectively. These results are, again, in qualitative
 545 agreement with predictions made on the basis of the simple static approach for the reaction in
 546 the gas phase predicting a negligible change in the free energy of reaction due to the
 547 temperature increase from 300 K to 500 K (see Section 3.1).

548

549 3.3.4 Structural analysis of TS_B at finite temperature

550 a) C-C and C-H bonds

551 The distribution of the C-C and C-H bonds in the PCP obtained in the MD runs are
 552 reported in Figure 8. The C-C and C-H bonds in the TS_B are typical for the constrained edge
 553 protonated cyclopropane and their averages are very similar to the values found for TS_B in
 554 the gas phase reaction determined in the static approach (see Section SVII).



555
 556 **Figure 8.** Probability distributions of selected C-C and C-H bond lengths in the transition states of (a)
 557 type B isomerization (TS_B), and (b) for type A isomerization (TS_A) determined using MD at 300 K
 558 (solid lines) and 500 K (dashed lines). For the sake of comparison, the static approach results for the
 559 gas phase reactions are also indicated by vertical dotted lines. Bottom panels show data determined
 560 for the series of static calculations for reactions in chabazite discussed in Section 3.2.

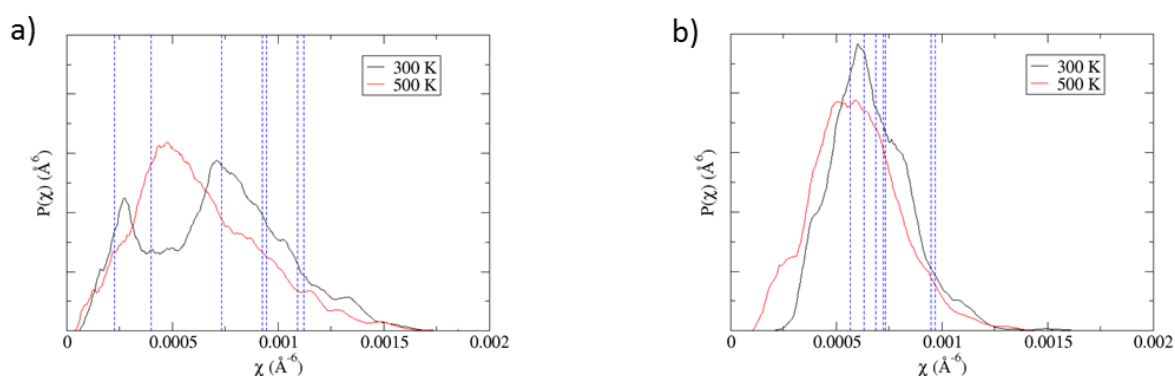
561
 562 Furthermore, the relation between the standard deviation of the bond length distribution and
 563 its effective force constant [74] allows us to conclude that the bond C^2-C^4 formed during
 564 reaction is stronger in transition state than that in reactant, while the other two bonds involved
 565 in the PCP formation (C^3-C^4 and C^2-C^3) are comparably strong (see Section SVII.1 and Table

566 S13) and this result is consistent with the tight TS loose reactant picture. The intramolecular
567 geometry of structures optimized in the zeolite are rather similar to the average MD structures
568 and this agreement indicates that the very large difference in energy and free energy between
569 relaxed structures is not due to intramolecular geometric features.

570

571 **b) Location of TS_B with respect to Al**

572 In Section 3.2 we showed that the electronic energy of transition states correlates with the
573 inverse distances between Al and C atoms (measured via parameter χ), which, in turn reflects
574 the variation in distribution of the molecule within the cavity of zeolite. In the constrained
575 molecular dynamics run of the transition state at 300 K (Figure 9-a), the parameter χ ranges
576 between 0.0005 \AA^{-6} and 0.0017 \AA^{-6} and the distribution of χ is bimodal with maxima at
577 $2.7 \cdot 10^{-4} \text{ \AA}^{-6}$ and $7.0 \cdot 10^{-4} \text{ \AA}^{-6}$.



578

579 **Figure 9.** Probability distribution of the sum of inverse distances between the framework Al and all C
580 atoms raised to the power of six (χ) determined for the transition state of type B (a) and type A (b)
581 isomerization in chabazite determined using MD at $T = 300 \text{ K}$ and 500 K . For the sake of comparison,
582 the static approach results for the reaction in chabazite are indicated by vertical dashed lines.

583 The various TS_B determined in the series of static calculations are located fall into different
584 parts of this distribution. At 500 K , the shape of the distribution changes and the dominant
585 peak is shifted towards longer distances (i.e. smaller χ). Obviously, such an effect cannot be

586 taken into account using a simple static approach based on the harmonic approximation
587 because the potential energy minimum structure is always the most likely configuration
588 regardless of temperature.

589

590 **3.4. Free energy calculations for type A isomerization reaction**

591 **3.4.1. Choice of the approximation to the reaction coordinate**

592 As described in Section 3.3.1, the parameter ξ used in free energy calculations of type B
593 isomerization has been constructed so as to cover also type A isomerization but the only
594 purpose of such a choice was to prevent the uncontrolled transformation of the product
595 configuration. Unfortunately, this approximation of reaction coordinate is not suitable for
596 calculations related to type A isomerization because it involves two C-H distances defined for
597 a specific hydrogen atom (H^a) which plays no particular role in this reaction. The undesired
598 consequence is that any rotation of the CH_3 group containing H^a would be artificially
599 hindered. In order to avoid such problems, we use for type A isomerization the following
600 approximation of reaction coordinate which is defined only via positions of carbon atoms,
601 and it is invariant with respect to the interchange of CH_3 groups attached to the same central
602 carbon atom:

$$\xi = \eta(C^2) - \eta(C^4), \quad (9)$$

603 where $\eta(C^i)$ is the coordination number [75] of central carbon atom C^i with respect to the
604 carbon atoms $C^1, C^3, C^5, C^6,$ and C^7 (the numbering of atoms is as in Figure 1-b), which we
605 defined as follows:

$$\eta(C^i) = \sum_{j=1,3,5,6,7} \frac{1 - \left(\frac{d(C^i - C^j)}{d_{ref}}\right)^9}{1 - \left(\frac{d(C^i - C^j)}{d_{ref}}\right)^{14}} \quad (10)$$

606 with $d_{ref} = 1.7 \text{ \AA}$ being the reference length for the C-C bond. During type A
607 isomerization, the reaction coordinate varies in the interval between -0.4 to 0.4 and $\xi^* = 0$
608 by symmetry.

609

610 **3.4.2. Characterization of reactant and product states**

611 As explained in Section 3.1, the reactant and product of type A isomerization are symmetry
612 equivalent. Because both states are equivalent to the product of type B isomerization, we
613 employ in this section the labeling used in Section 3.3 and designate the reactant/product
614 states of type A isomerization as P. The chosen reference state $\xi_{ref,P} = -0.35$ (see Equation
615 1) corresponds to a high-likelihood state in the free MD runs at both temperatures considered
616 in this study (see Figure S3). As the potential energy barrier for the transformation between
617 the six symmetry equivalent rotational isomers is only 3.0 kJ/mol (see Section 3.1),
618 straightforward MD simulations can be used to determine the probability density of the
619 reference state. The values of $\tilde{P}(\xi_{ref,P}) = g_P P(\xi_{ref,P})$ computed for T=300 K and 500 K are
620 2.45 and 2.25, respectively.

621

622 **3.4.3. Free energy calculations**

623 As in Section 3.3.3, the blue moon ensemble approach [67,68] has been used to determine
624 the term $\Delta A_{\xi_{ref,P} \rightarrow \xi_A^*}$. In our calculations, a mesh of eight integration points corresponding to
625 states distributed between the reference reactant ($\xi_{ref,P} = -0.35$) and the transition states
626 ($\xi_A^* = 0$) has been used. The full free energy profiles $A(\xi)$ computed for T=300 K and 500 K
627 (Figure 7) have been subsequently obtained by making use of the symmetry of the problem
628 ($A(-\xi) = A(\xi)$), which follows from the fact that the reactant and the product molecules are
629 symmetry equivalent. The values of the velocity term $|\dot{\xi}^*|$ ($5.68 \cdot 10^{12} \text{ s}^{-1}$ and $7.34 \cdot 10^{12} \text{ s}^{-1}$ for
630 T=300 K and 500 K, respectively) have been determined as described in Section SII. The

631 computed contributions of the term $\Delta A_{\xi_{ref,P} \rightarrow \xi^*} = A(\xi^*) - A(\xi_{ref,P})$ to the free energies of
632 activation of type A isomerization at 300 K and 500 K are 15.1 (± 0.8) kJ/mol and 14.0 (\pm
633 0.9) kJ/mol, respectively. Combined with the data presented in Section 3.4.2, the free
634 energies of activation computed using Equation 1 are 14.9 (± 0.8) kJ/mol and 15.0 (± 0.9)
635 kJ/mol for T=300 K and 500 K, respectively. Hence, the free energy of activation for type A
636 isomerization is, according to our simulations, basically independent on temperature, which is
637 in agreement with the conclusion made in Section 3.1, where a simple static approach for the
638 reaction in the gas phase was discussed.

639

640 **3.4.4 Structural analysis of TS_A at finite temperature**

641 **a) C-C and C-H bonds**

642 The analysis of the distributions of the C²-C³ and C³-C⁴ bonds shows that they are
643 both significantly looser than the chemical bond C²-C⁴, which is comparably strong as the C-
644 C bonds in the reactant (see Figure 8-b and Section SVII.2 and Table S13). Moreover, visual
645 inspection of the MD structures reveals that the methyl group shifted during the reaction
646 freely rotates (unlike the CH₃ group formed during type B isomerization). This is clearly
647 illustrated in Figure 8-b, where a narrow distribution of the C³-H^a bond centered at a typical
648 bonding distance (~ 1.1 Å) is found while the distribution for the non-bonding C⁴-H^a distance
649 is very broad because of rotations of the methyl group shifted during the reaction. This
650 analysis confirms that the transition state for type A isomerization, of corner-protonated PCP
651 nature, is much less constrained than that for type B isomerization, of edge-protonated nature.
652 Altogether, despite the apparent similarity in TS structures of type A and B isomerization
653 reactions (both TS are usually represented by very similar schemes in chemical textbooks),
654 both structures differ in the strength of C-C bonds which are formed or broken, and in the

655 specific role of the H transfer in TS_B , which in turn leads to significant differences in free
656 energy of activation and in the thermal dependence of the latter.

657 **b) Location of TS_A with respect to Al**

658 As in the case of type B isomerization, we explore the distribution of the TS_A within the
659 zeolite cavity by analyzing the parameter χ (see Section 3.2). As shown in Figure 9-b, χ
660 varies between $1.4 \cdot 10^{-4} \text{ \AA}^{-6}$ and $1.4 \cdot 10^{-3} \text{ \AA}^{-6}$ and the distribution shows one dominant
661 maximum which is shifted towards smaller χ with increased T ($6.1 \cdot 10^{-4} \text{ \AA}^{-6}$ (300 K) and
662 $5.5 \cdot 10^{-4} \text{ \AA}^{-6}$ (500 K)). As evident from Figure 9-b, most of the first order saddle points on the
663 PES determined in our static calculations (see Section 3.2) are located close to the maximum.
664 While our static transition state search identified two configurations corresponding to TS_A
665 with significantly larger than average χ (i.e. with shorter than average effective distances
666 between Al and C atoms), no configuration from the region $\chi < 5 \cdot 10^{-4} \text{ \AA}^{-6}$ has been found (see
667 Figure 9-b). The fact that the latter region is populated mainly at high T points once again at
668 the systematic failure of the naïve static approach to account for non-trivial thermal effects.

669

670 **3.5. On the atomic origin of the different kinetics of type A versus type B isomerization** 671 **reactions in zeolites**

672 Somewhat surprisingly at first sight, the results obtained using the sophisticated and
673 time-consuming MD simulations are in qualitative and even semi-quantitative agreement
674 with the calculations performed using the static approach for the gas phase reactions. Indeed,
675 the latter set of calculations predicted the correct thermal trends for free energies of activation
676 and of reaction for both temperatures, although the numerical values are overestimated by up
677 to 16 %. Such a qualitative agreement is possible because of the following reasons: (i) the
678 effect of interactions of molecule with CHA zeolite on reaction barriers is only modest, and
679 (ii) the approximations used in the static approach are reasonable when applied to relatively

680 small gas phase molecules. The point (i) can be understood because the CHA zeolite does not
681 directly participate in chemical reactions analyzed in this work, and the nature of interaction
682 between the CHA zeolite and the molecule does not change during the chemical reaction.
683 Thus, confinement effect is roughly the same for the reactants, the transition states and the
684 products in the case we are investigating. Note however that shifting from the CHA zeolite
685 (used here) to another framework, or from one kind of channel/cage to another one contained
686 within the same zeolite, the extent of the confinement effect is expected to change [76], likely
687 altering the catalytic performance. In particular, in the case of smaller cages or channels (such
688 as ZSM-22 for example, mono-dimensional 10 MR framework), one may expect a
689 differentiation of the zeolite/cation interactions depending on subtle steric constraint changes,
690 such as the one taking place in the course of the reactant \rightarrow transition state \rightarrow product
691 transformation. Similar differentiation may occur in the case of bulkier reactants as compared
692 to the C7 molecules considered here. The point (ii) follows from the fact that the harmonic
693 oscillator model used in the static approach performs rather well when describing vibrations
694 of the intramolecular degrees of freedom [77,78]. Furthermore, the size and shape of the large
695 CHA cavity where the reaction takes place restricts only very weakly the molecular rotations
696 in our case, and this modest restriction is similar for all stages of reaction. Hence also the
697 rotational contribution to free energy differences predicted by the gas phase model is
698 reasonable. Finally, the translational contribution computed using the static approach for a
699 gas phase molecule depends only on the molecular mass and the volume available for the
700 motion [79]. As both of these quantities are constant in the case of the monomolecular
701 reaction at the NVT conditions, the contribution of translational degrees of freedom to the
702 relative free energetics of a monomolecular gas phase reaction must vanish. In the case of
703 reaction in zeolite, the volume available for the translation motion of molecule remains
704 approximately constant during the reaction. Because also the nature of interaction between

705 the molecule and zeolite remains essentially unaltered, the contribution of translational
706 degrees of freedom also largely vanishes in the MD based calculations of free energy
707 differences for a monomolecular reaction in zeolite. In contrast, an attempt to describe
708 hindered rotations and translations of a molecule in zeolite by harmonic oscillator model, as it
709 is done when using the static approach in zeolite, necessarily fails because of large
710 contribution of low frequency vibrational modes to free energy and because of complexity of
711 underlying potential energy surface [29,30,36,46].

712 In our in-depth analysis of this problem, we considered for the first time all
713 components contributing to free energy of activation. We have shown that the very large
714 uncertainties in free energies of individual states, which are in the case of type B
715 isomerization as large as 40 kJ/mol, do not cancel significantly even when the corresponding
716 stationary points are carefully chosen so as to be linked by a common intrinsic reaction
717 coordinate. The uncertainty in computed free energy of activation can increase further if the
718 minima and TS configurations are obtained in independent relaxations, as it is often the case
719 in literature. For instance, the computed free energy barrier for the forward mode of type B
720 isomerization spreads over the interval between 36.4 kJ/mol to 97.3 kJ/mol.
721 Counterintuitively, therefore, a gas phase model is indeed likely to provide more reliable
722 results than a periodic model involving zeolite when the static approach is applied to a
723 monomolecular reaction.

724 The qualitatively correct static gas phase model of type A and B isomerization reactions
725 can be utilized in the interpretation of our MD results. Already from electronic activation
726 energies in gas phase static calculations (ΔA_{el} in table S3 and S4, 70.4 and 13.7 kJ.mol⁻¹ for
727 type B and A isomerization reactions, respectively), the slower rate of type B isomerization
728 with respect to type A isomerization can be deduced. The lower stability of TS_B can be
729 intuitively understood because a larger number of chemical bonds is formed or broken in type

730 B (C^2-C^4 , C^3-C^4 , H^a-C^3 , and H^a-C^4) than in type A (C^3-C^2 , C^3-C^4) isomerization and all those
731 bonds are significantly stretched in TS_B structures compared to the corresponding bond
732 lengths in reactant or product states, see Figure 1.

733 In the case of type B isomerization, the thermal dependence of free energy of activation is
734 almost exclusively due to the difference in intramolecular contribution to vibrational entropy
735 between reactant and transition state, which is an edge protonated cyclopropane. Such a result
736 is again a consequence of the fact that the atomic motions in transition state are more
737 constrained than those in reactant because a large number of strong chemical bonds are
738 formed or broken in TS_B . In the case of type A isomerization, the entropy of activation nearly
739 vanishes which results in a very small variation of the free energy of activation with
740 temperature. In contrast to type B isomerization, the transition state for type A isomerization
741 (a corner protonated cyclopropane) is not significantly more constrained than the reactant
742 because the shifted CH_3 group is bound to the rest of molecule (similar to neutral 2,3-
743 dimethyl but-2-ene) by only very loose bonds, which is evident also from the analysis of the
744 MD data (see Sections 3.3.4 and 3.4.4).

745 In the end, the edge position of the H^a in TS_B (edge-protonated PCP) has both
746 energetic and entropic consequences, causing its lower stability (despite independent stronger
747 bonds, as probed by the vibrational analysis) compared to less constrained TS_A . This is the
748 atomic origin of the much higher rate constants found in single-event kinetic models fitted for
749 type A isomerization with respect to type B isomerization [8,15,16].

750 **4. CONCLUSION**

751

752 In this work, a comprehensive ab initio investigation of isomerization reactions of 2,4-
753 dimethyl-pent-2-enium and 2,3,3-trimethyl-but-2-enium cations in chabazite is reported,
754 which provides atomic scale interpretation of the kinetic differences between type A and type

755 B isomerization of alkenes. The main impacts of our results in terms of understanding of
756 isomerization in heterogeneous catalysis are:

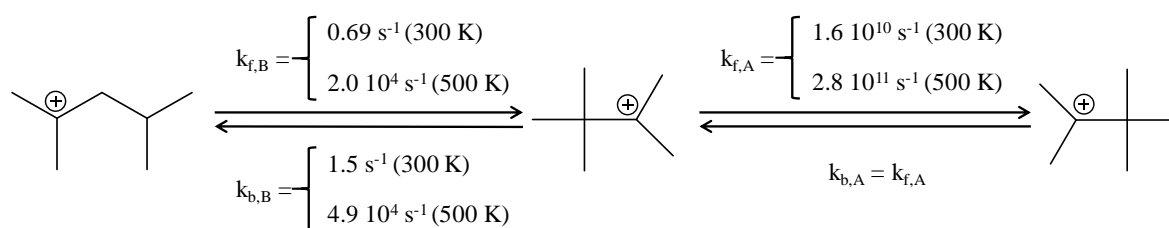
757 - The proper quantification of the respective free energy barriers of type A and type B
758 isomerization reactions of alkenes by ab initio molecular dynamics, provided here for the first
759 time. The reactions studied herein are the “building blocks” in practice for the key elementary
760 steps of the hydroisomerization of alkanes.

761 - The unraveling of the origins of the differences in terms of rate constants between
762 type A and B isomerization reactions, in terms of structure of the transition state. A priori,
763 both kinds of TS are protonated cyclopropanes, which makes the ranking in terms of stability
764 difficult without a fine investigation. Our investigation shows that the two TS are very
765 different in nature (tight for type B, an edge-protonated PCP, loose for type A, a corner-
766 protonated PCP), with direct impact on their free energy.

767 In practice, accurate free energy calculations have been performed by means of molecular
768 dynamics in combination with blue moon ensemble approach [67,68]. The problem with non-
769 ergodic sampling of reactant state due to slow transformation between individual rotational
770 isomers, often overlooked in literature, has been addressed. In the case of type B
771 isomerization, this problem is particularly serious since only one of three symmetrically non-
772 equivalent rotamers can directly undergo the atomic rearrangement associated with this
773 chemical reaction. In this work we proposed and applied a simple solution consisting in
774 explicit sampling of the slow skeletal rotation by the blue moon ensemble approach (other
775 techniques designed to study rare events, such as metadynamics or umbrella sampling, could
776 be used as well [43,80]). The resulting free energy profile is then used to determine the
777 likelihood of the active rotamer among all reactant configurations, which, in combination
778 with the probability density of an arbitrarily chosen reference state of the active rotamer,

779 allows for the determination of the corresponding contribution to free energy changes defined
780 with respect to a generic reactant state.

781 The free energies of activation and reaction computed using MD for type B isomerization
782 at T=300 K are 74.4 kJ/mol and 1.9 kJ/mol, respectively. Increasing temperature to 500 K,
783 which is closer to the conditions relevant for hydrocarbon transformations in zeolite [8,16],
784 the free energy barrier increases to 83.4 kJ/mol, while the free energy of reaction changes
785 only negligibly (3.7 kJ/mol). For type A isomerization, the free energy of activation
786 determined for T=300 K is significantly lower than that for type B isomerization and its
787 numerical value changes only negligibly with T (15.1 kJ/mol (300 K) and 14.0 kJ/mol (500
788 K)). The corresponding kinetic constants determined via the Eyring equation [81] are
789 reported in Scheme 1. Such rate constants, which are compatible in order of magnitude with
790 the rate constants of similar compounds in superacid media[17], are likely to be
791 representative of C7 type A and B isomerization of alkenes between two tertiary carbenium
792 ions.



794 **Scheme 1.** Kinetic constants at 300 K and 500 K for type B and A isomerization reactions.

795 The former result is consistent with the experimental observation that the measured
796 reaction rate for type A isomerization is several orders of magnitude higher than that for type
797 B isomerization [8,15,16]. As type A isomerization considered in this work leads to
798 formation of product that is symmetry equivalent to reactant, the free energy of reaction is, by
799 definition, zero at all temperatures.

800 A static calculation analysis appeared to be irrelevant when performed in the zeolite, due to
801 the many stable configurations of different energies that can be found, but insightful when
802 performed for gas phase reactions. Confinement effects indeed appeared to be comparable for
803 the reactants, the transition states and products in our case. The origin of the difference in rate
804 for type A versus type B isomerization reactions was identified on the basis of our
805 calculations: the transition state TS_A (a corner protonated PCP) has a loose structure, with
806 two large C-C bonds at the PCP, and free rotation of the moving methyl group, whereas TS_B
807 (an edge-protonated PCP) is much tighter due to the bridging hydrogen atom, and to the
808 many bonds that are formed or broken at this elementary step.

809 The simulation protocol developed within this work represents a powerful tool for the
810 investigation of isomerization reactions of alkenes in acidic zeolites and it is currently used to
811 elucidate the more complex mechanisms involving short-lived secondary carbenium ions
812 obtained from proton transfer from zeolite to alkenes. Moreover, the comparison of the
813 transformations of linear to mono-branched, then to di-branched carbenium ions, in
814 comparison with the present di-branched to tri-branched conversion, would be useful to get a
815 more complete view of the full isomerization reaction network. Notably, going beyond DFT
816 may be needed to reach chemical accuracy when describing non-classical species such as the
817 PCP transition states. This was shown for several reactions involving carbenium and
818 carbonium, up to the coupled-cluster level [82–85]. Transposing these approaches to alkene
819 isomerization is a clear perspective to the present work. However, combining this level of
820 calculation with the MD approach is currently prohibitive, so that the problem of the
821 identification by static calculations of ensemble of configurations in the zeolite and ensemble
822 of rotamers for each state in the zeolite needs to be addressed.

823

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