REGULAR ARTICLE

A theoretical study of the solvent effect on Diels-Alder reaction in room temperature ionic liquids using a supermolecular approach

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Abstract The Diels-Alder reaction between cyclopenta-diene and three dienophiles (acrolein, methyl acrylate and acrylonitrile) in different room temperature ionic liquids containing imidazolium-based cations ([HBIM]$^+$, [BMIM]$^+$ and [BM$_2$IM]$^+$) has been studied at the DFT level using a supermolecular approach. An analysis of the theoretical results shows that the ionic liquid cation coordination affects the equilibrium geometries and electronic structures of the reacting species throughout the reaction pathway leading to changes in reactivity and selectivity. They also indicate that the strong asynchronicity of the Diels-Alder reactions in ionic liquids is due to the polarisation effect of the cation.

Keywords Diels-Alder reaction · Ionic liquids ·
Ab initio calculations

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1 Introduction and method

In a previous paper [1] we studied the Diels-Alder reaction in room temperature ionic liquids (RTILs) using multi-parameter linear solvation energy relationships. The conclusions of the paper are that the hydrogen-bonding donation ability of the cation is important, both in selectivity and rates, when the dienophile is acrolein or methyl acrylate but not when the dienophile is acrylonitrile. This suggests that the capacity of the RTIL cation to establish a hydrogen bond with the dienophile is a key factor in the solvent enhancement of the reactivity of these systems.

The effect of the solvent on a chemical reaction can be considered at the theoretical level. Whereas for molecular solvents and non-specific interactions, continuum methods [2] can be used with good results, the nature of RTILs is very different from that of normal liquids, and the definition of an appropriate computational model requires re-consideration. We have a solvent that is constituted by two opposite charge ions with very different chemical natures. Even one of the ions is very large compared to molecular solvents. Other physical-chemical properties like viscosity present values in a range very different from those of common molecular solvents. The dielectric constant values for RTILs, the key parameter in continuum solvent models, are not well established: different methods give different values, but each method gives values very similar to all the RTILs investigated [3]. Despite this fact the effect of RTILs on chemical systems is very different even for apparently only slightly different solvents.

Thus we have a system that probably cannot be easily reduced to a continuum and with a specific solvent-solute interaction. In this case a supermolecular approach is necessary. In principle, supermolecules are not different from molecules from the theoretical point of view: all the
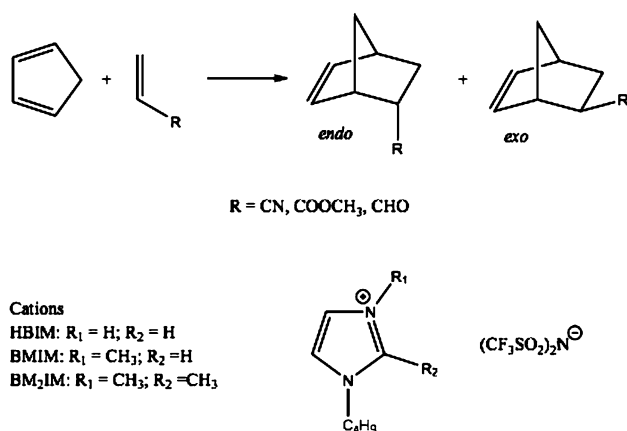
Scheme 1

ab initio molecular electronic structure methods do not use a pre-constituted molecular bonding scheme (except, in some cases, for the wave function initial guess).

The supermolecular system studied in this paper is constituted by three covalent-bonded molecules: the diene, the dienophile and an RTIL cation. This molecular system contains about 20 second-row atoms. The computational treatment of this system is not complex from the point of view of the intensive calculation costs (a large number of basic functions at a high level of theory) but from the point of view of extensive costs: is not easy to find a stationary point when there are a lot of loose internal coordinates like those that give the relative positions and orientations of the three molecules involved. To obtain the results and the structures presented in this paper there is a lot of work that cannot be (at the state of art) performed automatically by the software. Chemical sense was used to choose initial spatial arrangements of the molecules and some stop-and-go actions were needed with intermediate rearrangements to find the transition state related to the Diels-Alder reaction rather than to the transition state of a conformational equilibrium. When the cation dienophile relative position seemed strange or very different from those of similar cases, we investigated several starting points to validate the structure.

The Diels-Alder reaction considered here is a classical example of this type of reaction, and it is shown in the Scheme 1 along with the cations considered in this paper. The cyclic structure of the diene eliminates any issue about its conformation. We consider, in detail, the *endo/exo* selectivity for all the three dienophiles presented in the Scheme 1 in the presence of the [HBIM]$^+$, [BMIM]$^+$ and [BM$_2$IM]$^+$ cations.

2 Results and discussion

The reaction of cyclopentadiene with methyl acrylate, acrolein and acrylonitrile in three ionic liquids

([HBIM][Tf$_2$N], [BMIM][Tf$_2$N] and [BM$_2$IM][Tf$_2$N]) has been investigated through ab initio calculations at the B3LYP/cep-121g(d,p) level, using the Gaussian03 Package [4], with a supermolecular approach: a cation was enclosed in the model system to take account of the effect of the ionic liquid on the reaction. Since the three selected ionic liquids presented the same anion ([Tf$_2$N]$^-$ where Tf $=$ CF$_3$SO$_2$), which has been shown to be unable to give strong ion pairing [5], for reasons of computational costs we included in our investigation only one cation instead of an ion pair or a larger set of solvent ions. The use of this strategy is supported by the recent paper of Jorgensen et al. [6], in which the impact of acidic and basic 1-ethyl-3-methylimidazolium chloride-AlCl$_3$ ionic liquids upon cyclopentadiene and methyl acrylate Diels-Alder reaction rates has been investigated using QM/MM calculations. One of the main results of this paper is the observation that the effect of the cation on the reaction rate is more important than the effect of the anion.

Thus, to elucidate the effect of ionic liquids on the Diels-Alder reaction we performed calculations for the geometries of reagents (dienophile-cation complex + isolated diene), transition states and products, considering both the *endo* and *exo* stereochemistry, and the interaction of three imidazolium cations, [HBIM]$^+$, [BMIM]$^+$ and [BM$_2$IM]$^+$ with the three dienophiles used in the previous paper [1], bearing respectively on the double bond a nitrile (CN), a formyl (CHO) and methyl ester (COOCH$_3$) group. The corresponding calculations (reagents, TS and products), for both the *endo* and *exo* approaches, have been performed for the system consisting of the diene + dienophile alone, without inserting the ionic liquid cation. A total of 60 geometries have been optimized. Some of these optimization procedures, especially those related to cation-assisted transition states with *endo* stereochemistry, were very complex and required some stop-and-go actions, with manual rearrangement of the molecular structures, to avoid finding transition states related to relative torsions of several fragments and other spurious reaction coordinates. All the obtained structures for the TS geometries present a single imaginary frequency. Barriers, reaction heats and some relevant data related to the transition state geometries are reported in Table 1, including imaginary frequencies and some atom-atom distances. All the energetic results reported include zero-point energy correction.

As recently evidenced by Zhang et al. [7], calculations confirm that the Diels-Alder reaction in the presence of imidazolium salts proceeds via a concerted mechanism similar to the "uncatalyzed" reaction. Moreover, the energetic differences between reagents and transition states (reported in Table 1) for the *endo* and *exo* approach of the three dienophiles to cyclopentadiene in all the investigated ionic liquids are in agreement with the experimental data

Table 1 Relevant quantities from the ab initio calculations

IL cation dienophile	[HBIM]+			[BMIM]+			[BM₂IM]+			None		
	CN	CHO	CO₂CH₃	CN	CHO	CO₂CH₃	CN	CHO	CO₂CH₃	CN	CHO	CO₂CH₃
ΔG (R → TS)												
Exo	13.79	12.41	15.05	13.93	12.80	15.00	14.57	14.24	16.11	18.46	19.12	19.38
Endo	13.85	6.36	7.91	14.13	12.77	15.95	18.10	13.35	15.09	18.75	18.97	19.09
ΔG (P → TS)												
Exo	32.69	26.20	29.88	32.71	26.64	29.62	30.52	25.25	30.76	35.44	32.02	33.71
Endo	32.77	20.22	22.52	32.99	26.99	30.17	34.07	27.00	29.76	35.46	31.92	33.77
ΔG (R → P)												
Exo	−18.89	−13.79	−14.83	−18.78	−13.84	−14.61	−15.95	−11.01	−14.65	−16.98	−12.90	−14.33
Endo	−18.92	−13.86	−14.61	−18.86	−14.22	−14.22	−15.97	−13.65	−14.68	−16.71	−12.95	−14.68
ω_{TS}												
Exo	−404.8	−369.4	−398.4	−407.4	−377.7	−397.7	−413.6	−384.5	−408.0	−454.5	−438,5	−446.9
Endo	−411.2	−372.0	−378.7	412.7	−380.8	−383.8	−426.7	−390.7	−402.6	−453.9	−445.3	−450.0
C–C$_{terminal}$												
Exo	2.617	2.743	2.649	2.617	2.725	2.654	2.587	2.686	2.609	2.483	2.448	2.465
Endo	2.600	2.665	2.642	2.595	2.654	2.665	2.552	2.651	2.607	2.482	2.457	2.447
C–C$_{internal}$												
Exo	2.048	2.019	2.032	2.049	2.023	2.028	2.057	2.026	2.042	2.089	2.087	2.098
Endo	2.050	1.994	1.984	2.051	1.998	1.994	2.062	2.019	2.031	2.088	2.089	2.010
Coordination												
Exo	2–3	2–3	2–3	2–1	2–3	2–1	2–1	2–3	2–3	–	–	–
Endo	2–3	1–2	1–2	2–1	2–1	2–1	2	2–1	2–1	–	–	–
X–H$_{closer}$												
Exo	1.970	1.879	1.889	2.021	1.914	2.398	2.283	2.127	2.145	–	–	–
Endo	1.959	1.508	1.536	1.996	1.933	1.943	2.809[a]	2.153	2.159	–	–	–
X–H$_{farer}$												
Exo	3.108	2.437	2.532	2.887	2.438	1.943	2.325	2.168	2.223	–	–	–
Endo	3.298	3.435	3.466	3.253	2.34	2.379	–	2.156	2.164	–	–	–

[a] Energies in kcal/mol, lengths in Å, frequencies in cm⁻¹. R for reagents, P for products, TS for transition states. C–C$_{terminal}$ represents the distance between the diene carbon atom and the dienophile terminal carbon atom of the forming sigma bond in the TS. C–C$_{internal}$ represents the distance between the diene carbon atom and the dienophile internal carbon atom of the forming sigma bond in the TS. X is the heteroatom of the dienophile polar group: sp² oxygen for CHO and COOCH₃ and sp nitrogen for CN. The two hydrogen atoms that are coordinated to the heteroatom X are variable. Coordination elucidates the positions of the hydrogens interacting with the dienophile the numbers refer to the ring atoms: 1 is the nitrogen atom that is linked to the shortest aliphatic chain (no chain in [HBIM]+, methyl for [BMIM]+ and [BM₂IM]+); 2 is the carbon atom between the two nitrogen atoms of imidazolium ring; 3 is the nitrogen atoms bearing a butyl group in all investigated cations

[1]. A satisfactory correlation can be found between the activation energies calculated on the basis of the kinetic constants determined in [HMIM][Tf₂N], [BMIM][Tf₂N] and [BM₂IM][Tf₂N] and the sum of ΔG (R → TS) calculated for the *exo* and *endo* geometries in the same ILs. Nervertheless, the comparison of the values of ΔG (R → TS) for the *endo* and *exo* pathways, confirms the high selectivity in favor of the *endo* path for the reaction of cyclopentadiene with acrolein and methyl acrylate in [HBIM]+ based ionic liquid.

Finally, structural data reported in Table 1 confirm that the dienophile is coordinated to the most acidic hydrogen of the imidazolium ring; the hydrogen atom on nitrogen of the imidazolium ring, when it is present, or to the hydrogen

atom at C2 ring carbon. Only in the case of acrylonitrile in [BM₂IM]+ is the dienophile coordinated to the three hydrogen atoms of the methyl group at C2. Moreover, in agreement with the data of Zhang et al. the distance differences between the two forming C–C bonds in the TS indicate that asynchronicity of the reaction becomes more remarkable in the presence of the imidazolium cations.

In this paper, to avoid redundancy and a too large enumeration of the results we will discuss in detail only the two limiting cases having the highest *endo/exo* selectivity (6.36 vs. 12.41 kcal/mol), acrolein and methyl acrylate in [HBIM]+, which will be compared with a situation characterized by a low selectivity (18.10 vs. 14.57 kcal/mol), acrylonitrile in [BM₂IM]+. This latter situation is similar to

the uncoordinated reaction. All the other ionic liquids that we have studied can be considered to be intermediate situations between these. The transition state structures of the three mentioned reactions, in both the *endo* and *exo* stereochemistry, are reported in Fig. 1. It is evident that the presence of two acidic hydrogen atoms directly bounded to the imidazolium ring in [HBIM]$^+$ allows a closer spatial approach between the cation and dienophile than in the case of [BM$_2$IM]$^+$, where methyl groups prevent this approach.

To discuss the effect of the interaction of the [HBIM]$^+$ cation of the ionic liquid with the dienophile, we introduce here for the first time the clamp effect. The cation holds the dienophile like a clamp increasing the probability of dienophile/diene stacking that is mandatory for a reaction of
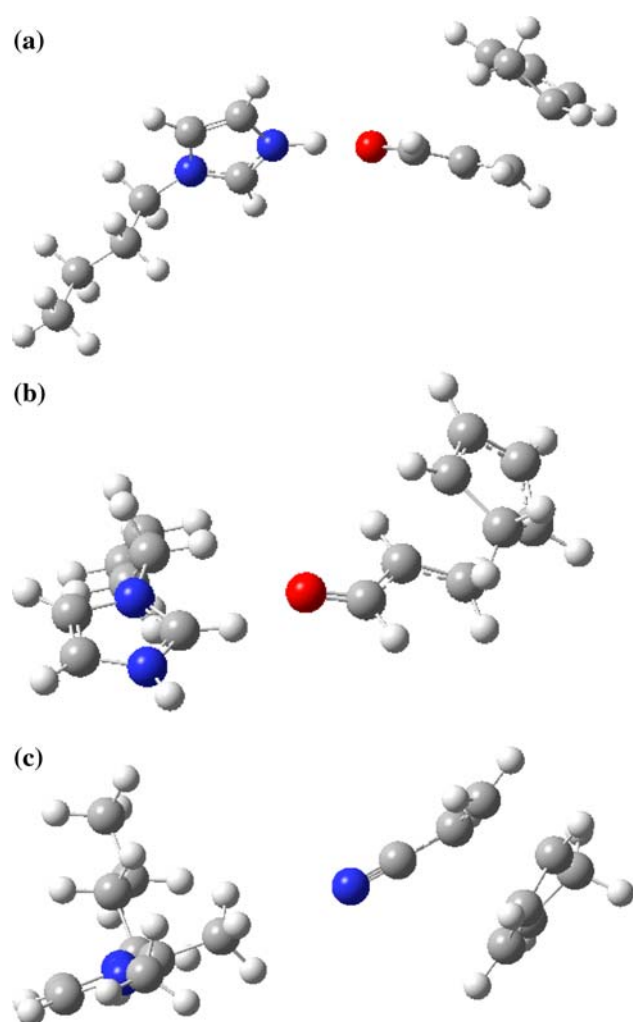

Fig. 1 Some transition state geometries. (**a**)/(**b**) *endo/exo* complex with the assistance of [HBIM]$^+$ cation. The relative orientation of the reactive complex diene/dienophile and of the cation is very different. (**c**) *Endo* complex with the assistance of the [BM$_2$IM]$^+$ cation. The presence of methyl group in position 2 increases the distance between cation and dienophile reducing the strength of the interaction

this kind. In the ionic liquid, the freedom of motion of the cation is strongly limited by the Coulombic interactions with the solvent bulk, which can be considered to act as a support. At the state of art the *clamp* effect is highly speculative; however, we have introduced the concept here because it is useful to explain some features of the Diels-Alder reaction in ionic liquids. The different ability of the ionic liquids to give clusters probably affects the ability of the ionic liquid to act as a support. Moreover, the strength of the "*clamp*" effect is related to the electrostatic and steric nature of the two actors. The polarity of the substituent(s) on the double bond (CHO > COOCH$_3$ > CN) determines the strength of the interaction of the dienophile with the cation, which is also affected by the number and the nature of hydrogens available [HBIM]$^+$ > [BMIM]$^+$ > [BM$_2$IM]$^+$). Two consequences of this effect on the Diels-Alder reaction can be evidenced:

1. The strong coordination of the dienophile with the cation leads to a polarization of the double bond of the dienophile increasing its reactivity. This can be evinced by the NBO population analysis and HOMO/LUMO energies. This argument will be examined more in detail in the following part of this paper.

2. The Diels-Alder reaction transition state involves the stacking of reagents. If one of the reagents is held firmly, the probability of a good stacking is increased. This effect is only a hypothesis at this stage of the research, since it cannot be confirmed by the static ab initio calculations like those presented in this paper, but the needs of a dynamical approach.

To evaluate the energetic effects of the cation dienophile coordination we report the differences between the energies of the reagents, transition states and of the products with and without the cation assistance, $E(\text{coord}) = E(\text{with cation}) - [E(\text{free}) + E(\text{cation})]$.

The results are reported as a histogram in Fig. 2. It is evident that the effect of cation dienophile coordination is stronger in the case of the *endo* arrangement, particularly in the reactions of acrolein and methyl acrylate in [HBIM]$^+$ ([HBIM]$^+$/CHO and [HBIM]$^+$/COOCH$_3$). The *exo* approach is characterized by a lower cation sensitivity; only in the case of [BM$_2$IM]$^+$ we observe a significantly reduced coordination ability. The stabilization effect on the transition state in the *endo* structures is probably due to the relative orientation of the π-system of the diene with respect to the activated dienophile.

Furthermore, the NBO [8] analysis of the TS structures shows that for [HBIM]$^+$/CHO and [HBIM]$^+$/COOCH$_3$, in both the *endo* and *exo* approaches, the formation of the C–C bond between the terminal dienophile C atom and the diene C atom is so advanced that the NBO algorithm found a localized bond orbital between them. The occupation

Fig. 2 Energetic estimation of the effect of the cation coordination on the Diels-Alder reaction. Energies in kcal/mol
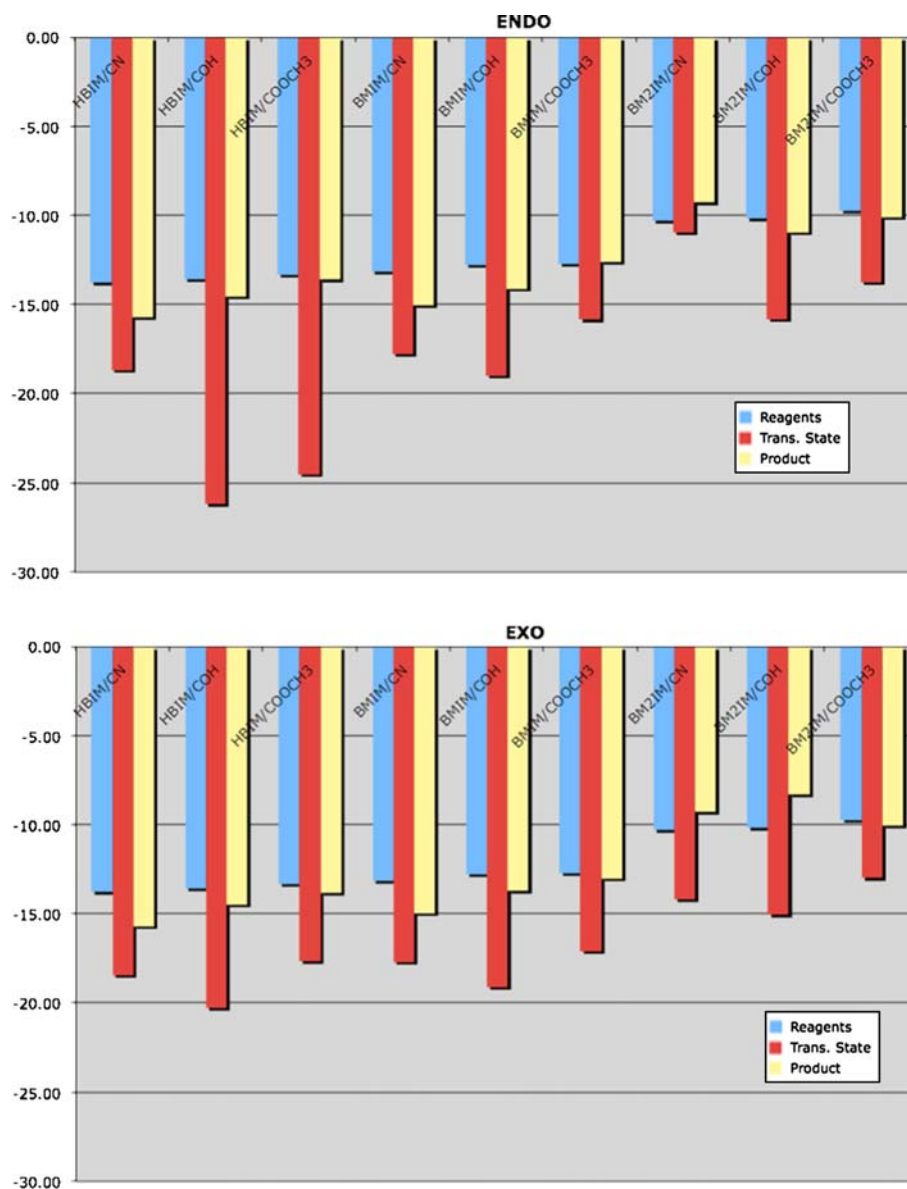
numbers for the C–C bonding orbital are 1.31814 (*exo* [HBIM]$^+$/COOCH$_3$), 1.32521 (*exo* [HBIM]$^+$/CHO), 1.66027 (*endo* [HBIM]$^+$/COOCH$_3$) and 1.66575 (*endo* [HBIM]$^+$/CHO). In all other cases, the NBO algorithm found three covalently bonded fragments corresponding to cation, diene and dienophile.

Finally, since the behavior of the Diels-Alder reaction can be easily understood in terms of the frontier molecular theory, in Fig. 3 we report a frontier orbital analysis. In this plot, the HOMO and LUMO energies for cyclopentadiene are reported and compared to the energies of the dienophile with and without cation coordination. It is evident that the coordination of the cation to dienophile decreases the gap between diene HOMO and dienophile LUMO leading to an increased chemical reactivity. These two orbitals

mix during the reaction path in the HOMO orbital of the transition state with a more favorable overlap in the *endo* structure with respect to the *exo* one.

3 Conclusions

The analysis of the computational results suggests that the ionic liquid cation coordination affects the equilibrium geometries and electronic structures of the reacting species throughout the reaction pathway leading to changes in reactivity and selectivity. They also demonstrate that the strong asynchronicity of the Diels-Alder reactions in ionic liquids is due to the polarization effect of the cation. The consequences of the "clamp" effect on the stacking

Fig. 3 The HOMO and LUMO energies for cyclopentadiene compared to the energies of the dieneophiles with and without cation coordination. Energies in Hartrees
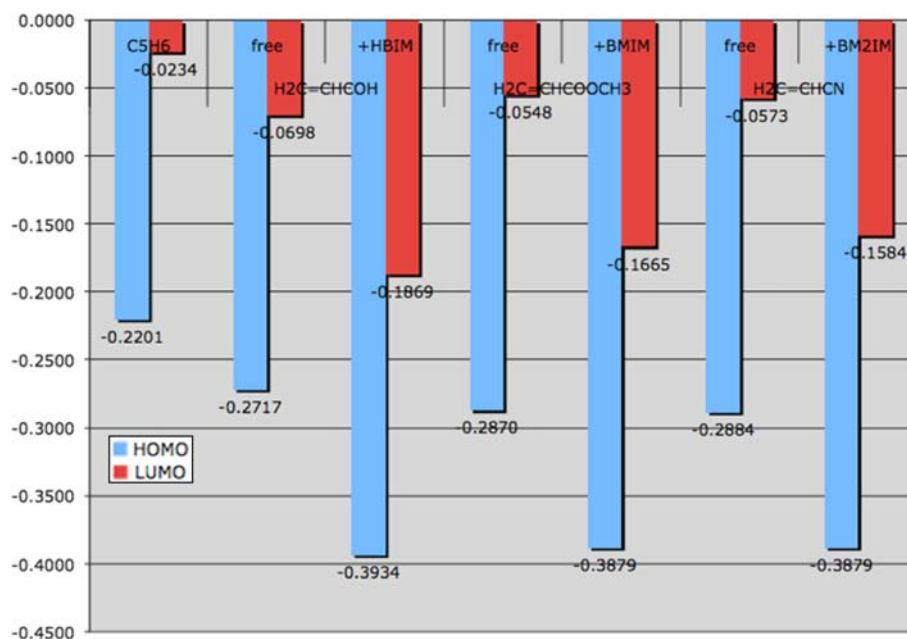
probability are only hypothetical at this stage, because they cannot be estimated by ab initio calculations but need a molecular dynamics approach; however, they could explain the experimental data.

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