Computational catalysis

Hydrogenation of carbon-heteroatom unsaturated bonds: An assessment of consistency of density functional methods[☆]

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ABSTRACT

Hydrogenation of unsaturated carbon-heteroatom bonds, C=X, is the general process for which we assess consistency of quantum chemical calculations in the context of $B(C_6F_5)_3$-catalyzed reduction of imines with H_2. According to the mechanism of the reaction, computational uncertainty of energies of hydrogenation of imines, i.e. the difference between results obtained with different methods, contributes to method-related uncertainties of the computed relative energies of key H_2-activating species. For this reason, it is desirable to know the magnitude of methodological dependence/uncertainty of energies of hydrogenation. Calculations were performed with a number of different density functionals, such as M05-2X, M06-2X, B3LYP, B3PW91, BH&HLYP, MPW1K, MPW1PW91, HCTH407 and PBE, on a number of relevant imines and ketones/aldehydes. Additionally, second-order Møller–Plesset perturbation theory was also evaluated. The results quantitatively reveal the manner in which the form of a method affects the calculated energy change and that there is substantial difference between results obtained with different methods even for structurally simple species.

1. Introduction

Metal-catalyzed addition of molecular hydrogen to unsaturated organic compounds is one of the most important and commonly applied methods in synthetic chemistry [1,2]. Reduction of imines and ketones/aldehydes, as well as nitriles, are common transformations employed to generate a variety of synthetic building blocks used in, for example, the pharmaceutical industry [1a,3,4].

Recent developments in metal-free catalysis, for instance the discovery of $B(C_6F_5)_3$-catalyzed reduction of imines (Eq. (1)) [5–7], highlighted a possibility to carry out hydrogenations without the use of expensive and potentially toxic metals. The ability of novel combinations of Lewis acids (LAs) and Lewis bases (LBs) to activate small molecules, most importantly H_2, has attracted particular interest. A significant number of mechanistic studies have been performed in order to understand fundamental principles which govern these new reactions [8–12]. In short, the so-called "frustrated Lewis pairs" (FLPs) [13], as well as a number of related LA–LB adducts [14], exhibit unusual reactivity due to "preorganization" within a donor–acceptor complex which facilitates bifunctional cooperation between the electron-rich and the electron-poor fragment [8a,12c]. It is noteworthy, that steric bulkiness of these fragments is of the essence for reactivity of FLPs. The rapidly growing interest in FLP-like systems is furthermore motivated by the ambition to advance metal-free hydrogen storage methodologies [15].

$$RN=CR'(H) \xrightarrow[\text{B}(C_6F_5)_3]{H_2} RN(H)CR'(H)_2$$

$$\mathbf{1} \qquad \mathbf{2} \qquad \mathbf{1'}$$
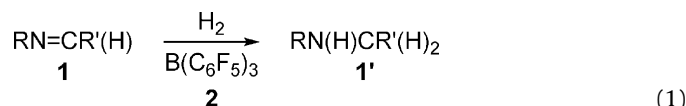
$$(1)$$

The usability of the correlated wave function theory (CWFT) methods drastically diminishes as the size of the model increases. The upper size of a system, for which a systematic improvement of the accuracy at and beyond the level of the second/fourth order Møller–Plesset perturbation theory (MP2/MP4) [16] is practically possible [17,18], i.e. Gaussian-3 theory or higher level CWFT approaches [19], pales in comparison with the size of an atomistic model of an FLP.

Since a tradeoff between accuracy and the required runtime of a density functional theory (DFT) based electron structure simulation with ca. 100–150 atoms is quite acceptable [20], DFT has been indispensable for quantum chemical studies of FLPs. Up to now, several density functional formulations such as B3LYP [21], M05-2X [22], PBE [23], MPW1K [24], BH&HLYP [31a] have been employed for the exploration of potential energy surfaces of FLP-mediated reactions [8,12,25,26]. Among those density functionals, PBE belongs to the family of gradient-corrected density functionals, while B3LYP, MPW1K, M05-2X and BH&HLYP are hybrid functionals with different amount of the
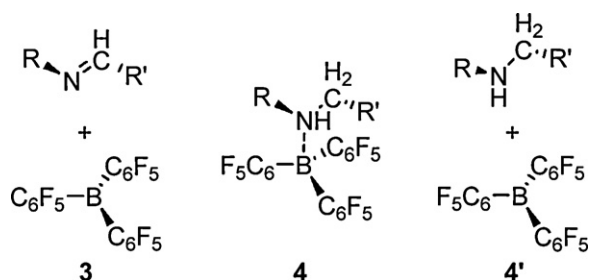

Fig. 1. Key imine/amine–B(C$_6$F$_5$)$_3$ complexes on the potential energy surface of Eq. (1); **3** and **4′** are H$_2$-activating FLPs. The equilibrium between **4** and **4′** is temperature-controlled.

Fig. 2. (A) Iminium and ammonium–B(C$_6$F$_5$)$_3$ ionic pairs, **5** and **5′**, respectively. (B) Simplified mechanism of catalytic reduction of imines for Eq. (1).

exact Hartree–Fock (HF) exchange varying from 20% up to 50% [27].

Despite refinement of density functional description of the exchange and the correlation interactions in a many-electron system, approximations are still required [28–31]. Different DFT forms are thought to perform better for different types of interactions and properties [32]; comparison of results, obtained with different density functionals, is therefore somewhat difficult [33–35]. In particular, that is the case for chemical reactions governed by combined covalent and non-covalent interactions, such as Eq. (1).

The peculiar aspect of Eq. (1) is that activation/"splitting" of H$_2$ by the FLP-like imine–B(C$_6$F$_5$)$_3$ complex **3** eventually affords an additional H$_2$-activating complex **4′** (Fig. 1) [6,8c,12b]. According to previous studies, a combination of non-covalent interactions, such as π–π stacking, C–H⋯π and C–H⋯F interactions, is responsible for dative bonding of the Lewis acid and Lewis base fragments in **3** and **4′**, as well as other currently known FLPs. From the chemical point of view, the only difference between **3** and **4′** is that the former features N=C double bond, which is saturated in the latter.
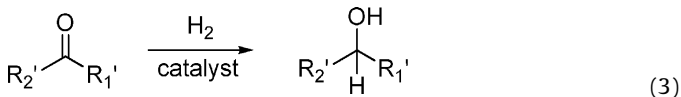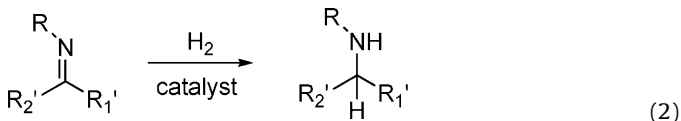

This brings us to the point of our study. Considering the overwhelming variety of density functionals, some of which are thought to offer better general description of combined (non-)covalent interactions, computational consistency of popular DFT formulations regarding needs to be evaluated. In this case we looked at a reaction important to FLPs, namely, the addition of H$_2$ to unsaturated systems (Eqs. (2) and (3)).

Specifically, we would like to know methodological variation of computed energy change in Eqs. (2) and (3) for those quantum chemical approaches which are applicable for studies of Eq. (1). In other words, evaluate in which way in the form of a method, suitable for Eq. (1), affects the calculated energy change in Eqs. (2) and (3).

For this reason and in order to avoid additional model/theory-dependences we employ a far less complex approach than the well-known Gaussian-3 theory; and although we deal with necessary thermochemical corrections, "raw" gas phase potential energies are used for the most of our study (see Section 3) [36].

Regarding practically appropriate WFT methods, the choice narrows down to MP2 (implementation-specific details regarding MP2 are given in Section 3). Considering previous studies and discussion in the literature, we have chosen 9 density functions, namely M05-2X, M06-2X, B3LYP, B3PW91, BH&HLYP, MPW1K, MPW1PW91, HCTH407 and PBE to be compared using a set of 12 imines and
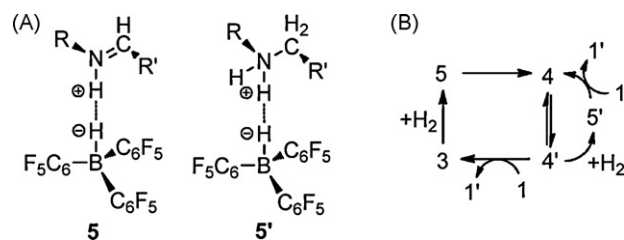
11 carbonyls. For those ketones/aldehydes which are part of the G3 set, we will also compare computational results and experimental data for enthalpies of formation.

2. Reduction of imines and relative energies of imine–borane and amine–borane FLPs

Before proceeding any further, it is instructive to review the mechanism of Eq. (1). According to the mechanism shown in Scheme 1, heterolytic cleavage of H$_2$ is performed by complexes **3** and **4′** (Fig. 1) [6,8c,12b]. In the first turnover of Eq. (1), only imines serve as basic partners of B(C$_6$F$_5$)$_3$ and H$_2$ is activated by the weakly bound FLP-like complex **3** affording ion pair **5** (Fig. 2). Nucleophilic attack of C-center by the BH$^-$ in **5** affords **4**. The process becomes catalytic at elevated temperature when the product amine is released to the solvent and B(C$_6$F$_5$)$_3$ can be re-used for H$_2$ activation. In subsequent turnovers, which involves direct- and non-covalently bonded amine–B(C$_6$F$_5$)$_3$ complexes **4** and **4′**, the key reaction steps are: (i) temperature-controlled equilibration between **4** and **4′**, association in the latter is due to dispersion interactions, (ii) uptake of H$_2$ by thermally activated amine–B(C$_6$F$_5$)$_3$ species **4′** affording **5′** and (iii) proton- and hydride-transfers from **5′** to an imine (Fig. 2).

Thus, **4′** is the product of an irreversible multi-step reaction **3** + H$_2$ → **4′**. Electronic energies of H$_2$-activating complexes **3** and **4′** could be defined as follows:

$$E[\mathbf{3}] = E[\mathbf{1}] + E[\mathbf{2}] + E_A[\mathbf{3}] \tag{4}$$

$$E[\mathbf{4'}] = E[\mathbf{1'}] + E[\mathbf{2}] + E_A[\mathbf{4'}] \tag{5}$$

where $E_A[\mathbf{3}]$ and $E_A[\mathbf{4'}]$ are corresponding association energies which are governed by non-covalent interactions. The electronic energy difference between **3** + H$_2$ and **4′** thus reads as follows:

$$\Delta E\{\mathbf{4'}, \mathbf{3} + H_2\} = \Delta E\{\mathbf{1'}, \mathbf{1} + H_2\} + \Delta E_A\{\mathbf{4'}, \mathbf{3}\}, \tag{6}$$

where $\Delta E\{\mathbf{1'}, \mathbf{1} + H_2\} = E[\mathbf{1'}] - E[\mathbf{1}] - E[H_2]$ and $\Delta E_A\{\mathbf{4'}, \mathbf{3}\} = E_A[\mathbf{4'}] - E_A[\mathbf{3}]$.

The former, $\Delta E\{\mathbf{1'}, \mathbf{1} + H_2\}$, describes the exothermicity of the reduction of imines to amines, while the latter, $\Delta E_A\{\mathbf{4'}, \mathbf{3}\}$, accounts for the difference between association energies of fragments in **3** and **4′**. Computational uncertainties of $\Delta E\{\mathbf{1'}, \mathbf{1} + H_2\}$ and $\Delta E_A\{\mathbf{4'}, \mathbf{3}\}$ are therefore two factors which limit the accuracy of Eq. (6). The latter, $\Delta E_A\{\mathbf{4'}, \mathbf{3}\}$, is affected by shortcomings of DFT-based treatment of weakly bound species.

Over the years, the issue of the DFT-based treatment of non-covalent interactions has received substantial attention and great improvement has been achieved, as confirmed by several thorough assessments [37]. Therefore, we will concentrate on the investigation of computational uncertainty of $\Delta E\{\mathbf{1'}, \mathbf{1} + H_2\}$ with respect to the formulation of a computational technique.
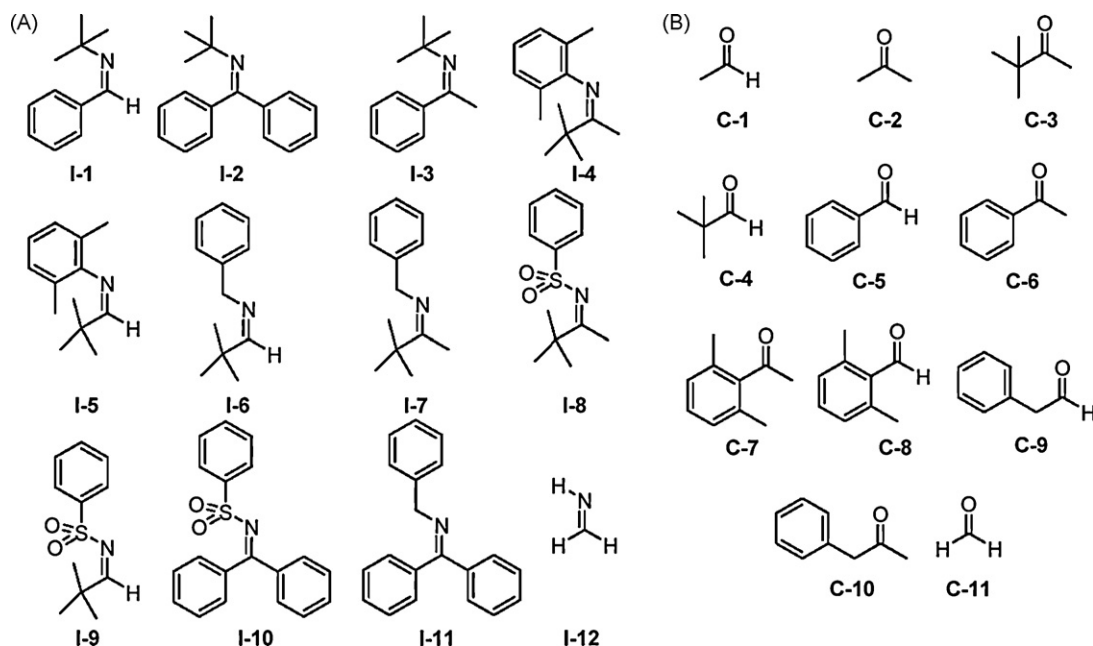
Fig. 3. (A) Imines I-1 to I-12 and (B) ketone/aldehydes C-1 to C-11 for Eqs. (2) and (3), respectively. C-1, C-2 and C-11 are part of the G3 set.

3. Computational details

All computations are performed with the Jaguar [38] package employing triple-zeta basis set, 6-311++G** [39,40], augmented with additional diffuse and polarization functions, and the molecular model system formally in gas phase. The following gradient-corrected and hybrid density functionals are employed in the present study: HCTH407 [41,42], PBE, M05-2X, M06-2X [35], B3LYP, B3PW91 [43], MPW1K, BH&HLYP and MPW1PW91 [44]. Regarding the second-order Møller–Plesset perturbation theory, the pseudospectral implementation of the so-called local MP2 (PS-LMP2) is used [45,46]. For convenience reasons, this PS-LMP2 technique is referred to as MP2.

All energies reported explicitly refer to lowest energy conformers of reacting species from Fig. 3 and corresponding products, all of which were independently searched with each aforementioned computational method. Every care has been taken to ensure consistency of geometries of all lowest energy conformers of all substrates and products across all DFT methods and MP2.

Enthalpy of formation (Table 2) has been computed as $H = E + ZPE + U + pV$, where E is the electronic energy at the DFT or MP2 level, ZPE is the zero point energy, and U is the internal energy. For the clarity of comparison, vibrational frequencies have been used for calculations of thermodynamic contributions to the enthalpy without any scaling.

In order to achieve quantitative understanding, the variation of results obtained with different methods is quantified with the help of the sample mean error, $ME = 1/N \sum_i x_i$, and the sample standard deviation, $\sigma^2 = [\sum_i x_i^2 - 1/N(\sum_i x_i)^2]/(N-1)$, where $x_i = \Delta E_i^X - \Delta E_i^Y$ and ΔE_i^X and ΔE_i^Y are energy difference between products and reacting species in Eqs. (2) and (3) computed with the methods X and Y; summation runs over all data points in a sample (12 imines and 11 carbonyls, respectively, see Fig. 3). A standard deviation is a measure of the dispersion of the data points of the sample with respect to the mean value and thus is a measure of dispersion of the results obtained with the method Y with respect to those obtained with the method X.

4. Energy change for imine to amine and carbonyls to alcohols reduction with H_2: comparison of computational techniques

In order to quantitatively assess the relation between the form of a computational technique and the calculated energy change in Eq. (2), a series of imines were selected all of which, except **I-12**, were employed in the original experimental study which reported the discovery of Eq. (1) (Fig. 3A). For completeness we have also computed the electronic energy change for the hydrogenation of a series of ketones/aldehydes (Fig. 3B). The complete account of computed electronic energies for Eqs. (2) and (3) is available in the Supporting Information.

Considering the combined inductive and resonance effects, the expected changes of the exothermicity of the hydrogenation reactions (Eqs. (2) and (3)) for substrates with different substituents is reproduced by all methods (Fig. 4). Despite the qualitative agreement between different methods, broad variation of results is quite apparent.

In order to get an idea about internal consistency of DFT methods, B3LYP was chosen as a reference in Fig. 5, as well as in Table 1. The discrepancy between DFT methods appears to be significant if

Table 1
Summary of method-dependences of $\Delta E^{B3LYP} - \Delta E^Y$ for the reduction of a series of imines (N=C) and carbonyls (O=C); Y = M05-2X, M06-2X, B3PW91, BH&HLYP, MPW1K, MPW1PW91, HCTH407 and PBE. All energies are in kcal/mol.

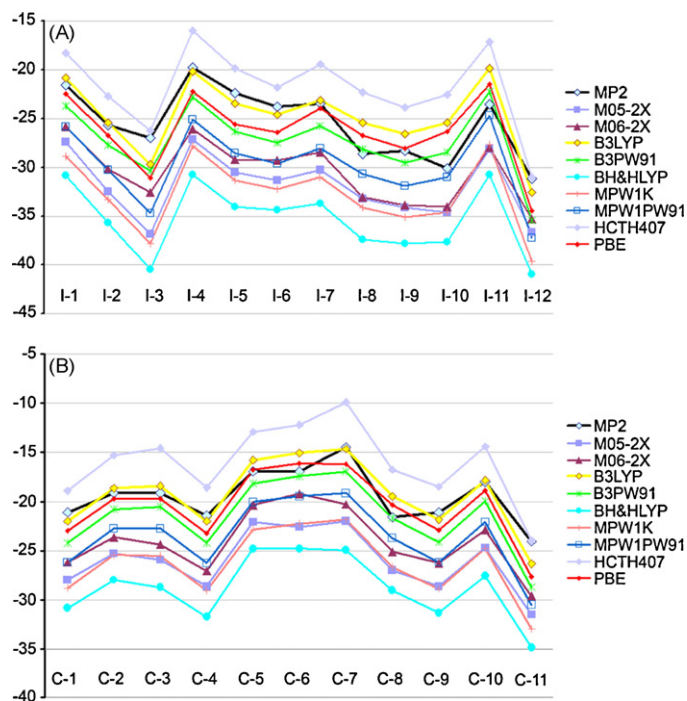|	M05-2X	M06-2X	B3PW91	BH&HLYP	MPW1K	MPW1PW91	HCTH407	PBE
ME(N=C)	7.13	5.73	2.56	10.62	8.04	5.05	−2.99	1.54
σ(N=C)	1.21	1.91	0.65	0.98	0.54	0.24	0.70	0.41
ME(O=C)	6.76	4.81	2.23	9.48	6.98	4.27	−3.28	1.14
σ(O=C)	0.74	0.79	0.09	0.56	0.19	0.11	0.65	0.18

Fig. 4. Overview of the computed energy change for Eqs. (2) (top) and (3) (bottom) for all imines and ketones/adehydes from Fig. 3. All energies are in kcal/mol.

judged by ME. The difference between results obtained with different methods could exceed 13 kcal/mol (HCTH407 *versus* BH&HLYP). On average, the discrepancy of results obtained with different hybrid functionals is 8.1 kcal/mol.

The amount of the exact HF-exchange included in the hybrid density functional form does seem to have significant effect on the calculated exothermicity of the hydrogenation, as readily seen from the results presented in Fig. 4 which are not biased by the choice of the reference (see also Fig. 5 and Table 1). The change of the correlation functional from LYP to PW91 increases exothermic on average by ca. 2 kcal/mol (B3LYP *versus* B3PW91). The MPW1K functional behaves quite similarly to M05-2X for all tested substrates. The lowest exothermicity of the hydrogenation of all tested substrates is obtained with the HCTH407 functional.

Nevertheless, the sample standard deviations (Table 1) suggest that nearly all methods are quite B3LYP-like, perhaps except functionals from the Minnesota-family. Among the methods tested, MPW1PW91 exhibits the lowest dispersion of results as compared to B3LYP and it is closely followed by the PBE and MPW1K functionals. Although the Minnesota-type functionals disperse from B3LYP the most, the standard deviations do not exceed 2 kcal/mol (see Table 1).

As pointed out earlier, although the exact form of the density functional formulations does affect the calculated energy change in Eqs. (1) and (2) to a significant extent, the distinction between density functionals is much less pronounced from the statistical point of view, e.g. standard deviations in Table 1. It is therefore intuitively reasonable to look at all DFT results from a viewpoint of a significantly different method, such as MP2. But before we pro-

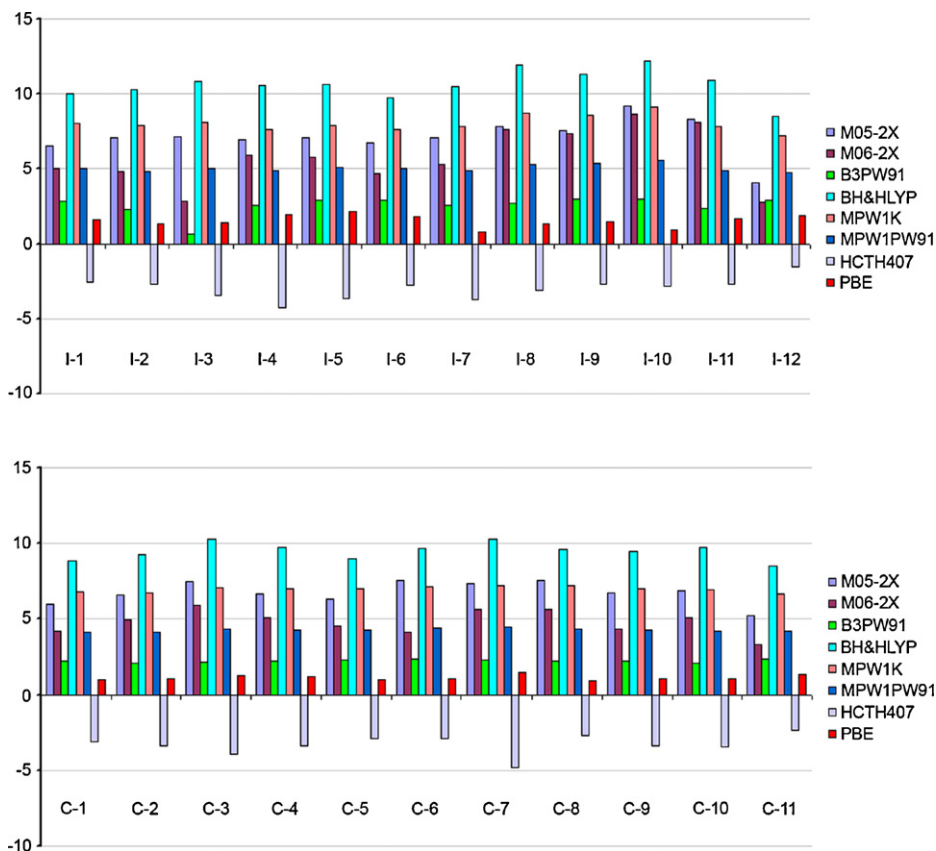**Fig. 5.** Differences between the B3LYP and other DFT methods, $\Delta E^{B3LYP} - \Delta E^{Y}$, for the reduction of imines (top) and ketones/aldehydes (bottom); Y = M05-2X, M06-2X, B3PW91, BH&HLYP, MPW1K, MPW1PW91, HCTH407 and PBE. All relative electronic energies are in kcal/mol.

Table 2
The difference between calculated and experiment-based total enthalpy change in Eq. (3) for C-1, C-2 and C-11 from Fig. 3. Experimental enthalpies of formation from the G3 set are used to for the experiment-based reference. All energies are in kcal/mol.

|	C-1	C-2	C-11	Averaged
Experimental	−16.5	−13.3	−22	
B3LYP	3.082	3.899	3.505	3.495
MP2	0.012	0.075	−0.117	−0.0103
MPW1K	−4.710	−3.650	−3.872	−4.077
M05-2X	−3.048	−3.553	−1.085	−2.562
M06-2X	−1.256	−1.893	0.797	−0.784
B3PW91	1.295	1.835	0.920	1.349
BH&HLYP	−5.918	−5.242	−8.865	−6.675
MPW1PW91	−1.621	−0.653	−0.869	−1.048
PBE	2.385	2.858	2.344	2.529
HCTH407	6.386	7.445	6.223	6.685

ceed, it is instructive to compare calculated and experiment-based changes in enthalpy for Eq. (3). Experimental values of C-1, C-2 and C-11 (Fig. 3) can be obtained from the G3 test set (Table 2). The MP2 method scores very good; the absolute deviation from the experiment is only 0.011 kcal/mol, 0.075 kcal/mol and 0.12 kcal/mol for C-1, C-2 and C-11, respectively. All DFT methods have far larger errors, although they remain fairly constant across different substrates.

Although we do not regard MP2 as a benchmark quality method, it is compelling to assess different DFT methods from the point of view of the MP2. At first glance, B3LYP does not deviate much from MP2 within the tested set of imines and carbonyls; the absolute minimum/maximum deviations from MP2 are 0.23/4.66 kcal/mol and 0.17/2.27 kcal/mol, respectively. The mean deviations are only −0.7 kcal/mol and −0.17 kcal/mol. However, the dispersion of B3LYP results is quite larger, σ = 2.23 kcal/mol and 1.29 kcal/mol.

The dispersion of B3LYP energies with respect to MP2 reported in a previous study of the reduction of a series of $R_2P = BR'_2$ species with H_2 [12c], which is to some extent analogue to Eq. (2), is similar to the herein reported results. Comparison of B3LYP and MP2 revealed that B3LYP on average predicts lower barrier heights by 6.5 kcal/mol with σ = 1.78 kcal/mol. Concerning the exothermicity of the reduction of B=P bond the mean deviation of B3LYP from MP2 was 2.03 kcal/mol with σ = 1.80 kcal/mol [12c] (Fig. 6).

The density functional M05-2X developed by Truhlar, has been shown to provide an improved description of non-covalent interactions and consequently it has been used in a number of studies of H_2 activation by FLP-like systems. As compared to MP2, the M05-2X predicts larger total energy change of hydrogenation of imines and carbonyls on average by 6.43 kcal/mol and 6.59 kcal/mol, respectively. The corresponding standard deviations are only 1.62 kcal/mol and 0.86 kcal/mol. The newer functional, M06-2X, exhibits smaller mean and standard deviations compared to M05-2X for the reduction of imines, ME = 5.03 kcal/mol and σ = 0.91 kcal/mol. However, in the case of the reduction of carbonyls, M05-2X results have somewhat smaller dispersion, 0.86 kcal/mol versus 1.12 kcal/mol, respectively. It is noteworthy that from purely statistical point of view, M06-2X is in closer resemblance to MP2 compared to B3LYP (compare the corresponding standard deviations in Tables 1 and 3).

Recent test of various forms of density functional revealed that BH&HLYP belongs to the category of functionals with the mean absolute error of less than 1 kcal/mol versus MP2 for a broad range of non-bonded interactions [47], in some cases it even allowed to obtain accuracy that rivaled higher correlated methods [48]. However, with respect to the test reaction, Eq. (2), the minimal and maximum deviations of BH&HLYP from the MP2 result are 7.21 kcal/mol and up to 13.52 kcal/mol, respectively, with the mean value of 9.9 kcal/mol. The standard deviation is 1.91 kcal/mol which
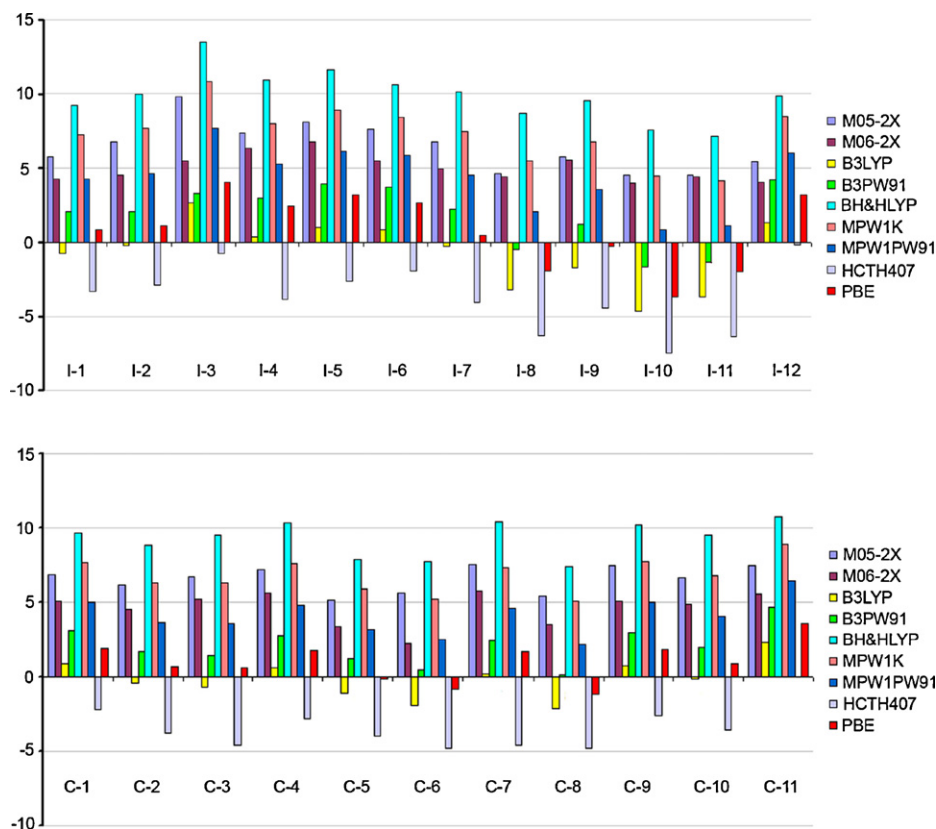
Fig. 6. Differences between the DFT- and MP2-based energy changes, $\Delta E^{MP2} - \Delta E^{DFT}$, for reduction of imines (top) and ketones/aldehydes (bottom). All relative electronic energies are in kcal/mol.

Table 3
Summary of methodological dependence of $\Delta E^{\text{MP2}} - \Delta E^{\text{DFT}}$ for the reduction of a series of imines (N=C) and carbonyls (O=C). All energies are in kcal/mol.

	M05-2X	M06-2X	B3LYP	B3PW91	BH&HLYP	MPW1K	MPW1PW91	HCTH407	PBE
ME(N=C)	6.43	5.03	−0.70	1.86	9.92	7.34	4.35	−3.69	0.84
σ(N=C)	1.62	0.91	2.23	2.03	1.73	1.91	2.10	2.24	2.45
ME(O=C)	6.59	4.64	−0.17	2.07	9.32	6.81	4.11	−3.45	0.97
σ(O=C)	0.86	1.12	1.29	1.31	1.16	1.17	1.25	1.45	1.38

is somewhat larger than that for M05-2X but still smaller than that for B3LYP. Concerning Eq. (3), the mean deviation of results is 9.93 kcal/mol and the corresponding σ is closer to that of B3LYP.

The search for density functional form suited for computing kinetics of chemical reactions resulted in a number of successful DFT methods, the MPW1K density functional being one of them. The MPW1K has also been reported to perform rather well, at least much better than B3LYP, for reactions which proceed *via* proton-coupled electron transfer or hydrogen-atom transfer mechanisms [49]. The former is somewhat similar to the process of heterolytic cleavage of H_2 by **3** and **4′**, which is essentially the proton-coupled hydride abstraction. Electron transfer from the lone electron pair of the Lewis base to the empty $\sigma^*(H_2)$ orbital and the electron transfer from $\sigma(H_2)$ orbital to the empty p orbital on boron occurs simultaneously. In our case, MPW1K, as well as MPW1PW91, perform similarly to M05-2X (see Table 3).

The two gradient-corrected functional forms, the PBE and HCTH407 exhibit comparable behavior. While PBE delivers results which are over or below the MP2 benchmark depending on the substrate, the HCTH407 consistently predicts much lower exothermicity. The distribution of deviations with respect to MP2 is characterized by $\sigma = 2.44$ kcal/mol and 2.23 kcal/mol for these methods, respectively.

In order to increase the accuracy of a computed energy, it is quite common to perform a single point MP2 calculation employing the geometry obtained with a DFT method. Although this combined DFT/MP2 method might not be practical for computational screening of potential energy surfaces of large systems, it is instructive to employ such an approach in those cases where DFT gives large deviation from the MP2 result. Single point MP2 calculations were preformed using geometries obtained by BH&HLYP, M05-2X and MPW1K for **I-3** (the case where the energy difference from MP2 is the greatest). As expected, the combined approach delivered results which were much closer to the pure MP2 and were largely independent on the form of the density functional which was employed for the geometry optimization: $\Delta E^{\text{MP2}} - \Delta E^{\text{DFT/MP2}} = 3.43$ kcal/mol, 3.35 kcal/mol and 3.39 kcal/mol for geometries obtained with BH&HLYP, M05-2X and MPW1K, respectively. The remaining difference between ΔE^{MP2} and $\Delta E^{\text{DFT/MP2}}$ results for Eq. (2) is due to the fact that all three DFT methods somewhat underestimates the C=N and C−N bond length as compared to those obtained with MP2 (see details in the Supporting Information).

5. Discussion and conclusions

In general, use of different methods for quantum chemical studies of a chemical process raises a concern about method-related dependence of the corresponding potential energy profile. The novel case, for which different aspects of method-related dependences are unclear, is the $B(C_6F_5)_3$-catalyzed reduction of imines with H_2. To address one of those, we employed nine different density functional forms (HCTH407, PBE, M05-2X, M06-2X, B3LYP, B3PW91, MPW1K, BH&HLYP, and MPW1PW91) and the second-order Møller–Plesset perturbation theory (MP2) for quantitative assessment of method-related variance of the energy change for hydrogenations of imines and ketones/aldehydes.

We have found that the aforementioned energy change is indeed quite method-sensitive. As we show in our study, this could be a concern for the comparison of relative energies of H_2-activating species, namely dative imine–$B(C_6F_5)_3$ and amine–$B(C_6F_5)_3$ couples, computed with different DFT methods. However, it appears that this concern could be alleviated by exploiting a better trend-wise accuracy of DFT methods.

Compared to the most popular density functional B3LYP, other tested hybrid functionals predict higher exothermicity of the hydrogenation. On average, the difference between results obtained with different hybrid functionals is ca. 8.1 kcal/mol. Among gradient-corrected functionals, PBE seems to give results that are close to those obtained with B3LYP and B3PW91, only HCTH407 stands out by predicting much lower exothermicity than other tested functionals. However, from a statistical point of view, all tested DFT methods appear to be much alike. We arrived at this conclusion by analyzing the standard deviation obtained with different functionals. Regarding the hydrogenation of imines, σ varies from ca. 0.24 kcal/mol up to ca. 1.9 kcal/mol, depending on the form of the density functional. The trend-wise agreement among various DFT methods is even better for hydrogenation of ketones/aldehydes.

We have also considered DFT results from the perspective of the MP2 method (although we have not regarded MP2 as a benchmark quality method). According to the calculations there is a considerable similarity between the statistical behavior of the MP2 and various DFT methods. Standard deviations of results obtained with DFT methods, relative to MP2, do not exceeding 2.5 kcal/mol for hydrogenation of imines (approximately only half of that for the hydrogenation of carbonyls).

Furthermore, for the hydrogenation of imines, the most MP2 like results in the sense of the standard deviation, were obtained with M06-2X, $\sigma = 0.91$ kcal/mol, followed by M05-2X, $\sigma = 1.62$ kcal/mol. For the hydrogenation of ketones/aldehydes, M05-2X predicts energies of the hydrogenation reaction with $\sigma = 0.856$ kcal/mol with respect to MP2, followed by M06-2X with $\sigma = 1.12$ kcal/mol. This is particularly interesting considering that both functionals reportedly offer generally improved description of non-covalent interactions. Although our findings point out disturbing method-related variation of the calculated energy change of a rather simple reaction, they also highlight a considerably trend-wise accuracy of DFT methods which could be exploited in mechanistic studies.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2010.03.001.

References

[1] (a) J.G. de Vries, C.J. Elsevier, The Handbook of Homogeneous Hydrogenation, Wiley–VCH, Weinheim, 2007;

(b) E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, Springer, Berlin, 2004;
(c) G.W. Parshall, S.D. Ittel, Homogeneous Catalysis: The Applications and Chemistry of Catalysis by Soluble Transition Metal Complexes, second ed., Wiley, 1992.

[2] (a) G. Zassinovich, G. Mestroni, Chem. Rev. 92 (1992) 1051;
(b) C.F. de Graauw, J.A. Peters, H. van Bekkum, J. Huskens, Synthesis (1994) 1007;
(c) J.M. Brunel, Tetrahedron 63 (2007) 3899;
(d) M. Wills, in: P.G. Andersson, I.J. Munslow (Eds.), Imino Reduction by Transfer Hydrogenations in Modern Reduction Methods, Wiley–VCH, Weinheim, 2008, pp. 271–296;
(e) H. Adolfsson, in: P.G. Andersson, I.J. Munslow (Eds.), Modern Reduction Methods, Wiley–VCH, Weinheim, 2008, pp. 341–362;
(f) M.K. Whittlesey, Compr. Coord. Chem. II 9 (2004) 265;
(g) T.V. RajanBabu, A.L. Casalnuovo, T.A. Ayers, N. Nomura, J. Jin, H. Park, M. Nandi, Curr. Org. Chem. 7 (2003) 301.

[3] (a) M.L. Clarke, G.J. Roff, in: J.G. de Vries, C.J. Elsevier (Eds.), The Handbook of Homogeneous Hydrogenation, Wiley–VCH, Weinheim, 2007, p. 413;
(b) W. Tang, X. Zhang, Chem. Rev. 103 (2003) 3029;
(c) S. Kobayashi, H. Ishitani, Chem. Rev. 99 (1999) 1069.

[4] (a) J.S.M. Samec, J.-E. Bäckvall, P.G. Andersson, P. Brandt, Chem. Soc. Rev. 35 (2006) 237;
(b) S. Gladiali, E. Alberico, Chem. Soc. Rev. 35 (2006) 226.

[5] D. Chen, J. Klankermayer, Chem. Commun. (2008) 2130.

[6] P.A. Chase, T. Jurca, D.W. Stephan, Chem. Commun. (2008) 1701.

[7] We have also computationally addressed a possibility of an analogous catalytic process for Eq. (2), see J. Nyhlén, T. Privalov, Dalton Trans. 29 (2009) 5780.

[8] (a) T.A. Rokob, A. Hamza, A. Stirling, T. Soos, I. Papai, Angew. Chem. Int. Ed. 47 (2008) 2435;
(b) A. Stirling, A. Hamza, T.A. Rokob, I. Papai, Chem. Commun. (2008) 3148;
(c) T.A. Rokob, A. Hamza, A. Stirling, T. Soos, I. Papai, J. Am. Chem. Soc. 131 (2009) 2029.

[9] (a) Y. Guo, S. Li, Eur. J. Inorg. Chem. (2008) 2501;
(b) S. Li, Y. Guo, Inorg. Chem. 47 (2008) 6212.

[10] A. Staubitz, M. Besora, J.N. Harvey, I. Manners, Inorg. Chem. 47 (2008) 5910.

[11] (a) V.S. Nguyen, M.H. Matus, D.J. Grant, M.T. Nguyen, D.A. Dixon, J. Phys. Chem. A 111 (2007) 8844;
(b) G. Gopakumar, V.S. Nguyen, M.T. Nguyen, J. Mol. Struct.: Theochem. 811 (2007) 77.

[12] (a) T. Privalov, Dalton Trans. 8 (2009) 1253;
(b) T. Privalov, Eur. J. Inorg. Chem. (2009) 2229;
(c) J. Nyhlén, T. Privalov, Eur. J. Inorg. Chem. 19 (2009) 2759.

[13] (a) L. Cabrera, G.C. Welch, J.D. Masuda, P. Wei, D.W. Stephan, Inorg. Chim. Acta 359 (2006) 3066;
(b) G.C. Welch, J.D. Masuda, D.W. Stephan, Inorg. Chem. 5 (2006) 478.

[14] For current reviews see;
(a) D.W. Stephan, Org. Biomol. Chem. 6 (2008) 1535;
(b) D.W. Stephan, Dalton Trans. (2009) 3129.

[15] (a) S. Orimo, Y. Nakamori, J.R. Eliseo, A. Züttel, C.M. Jensen, Chem. Rev. 107 (2007) 4111;
(b) V.V. Struzhkin, B. Militzer, W.L. Mao, H. Mao, R.J. Hemley, Chem. Rev. 107 (2007) 4133;
(c) A.J. Esswein, D.G. Nocera, Chem. Rev. 107 (2007) 4022;
(d) R.S. Kumar, E. Kim, O. Tschauner, A.L. Cornelius, M.P. Sulic, C.M. Jensen, Phys. Rev. B 75 (2007) 174110;
(e) G.J. Kubas, Chem. Rev. 107 (2007) 4152;
(f) see also Ref. [10] and references therein.

[16] C. Møller, M.S. Plesset, Phys. Rev. 46 (1934) 618.

[17] The runtime of conventional MP2 algorithms scales as nN^4, where N is the number of basis functions and n the number of occupied orbitals. Modern MP2 implementations have much improved scaling with system size, $\sim N^{2.7}$, for a wide range of mid to large size basis sets.

[18] R.J. Bartlett, J. Chem. Phys. 93 (1989) 1697.

[19] L.A. Curtiss, K. Raghavachari, P.C. Redfem, V. Rassolov, J.A. Pople, J. Chem. Phys. 109 (1998) 7764.

[20] L.A. Curtiss, K. Raghavachari, P.C. Redfem, V. Rassolov, J.A. Pople, J. Chem. Phys. 112 (2000) 7374.

[21] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.

[22] (a) Y. Zhao, N.E. Schultz, D.G. Truhlar, J. Chem. Theory Comput. 2 (2006) 364;
(b) Y. Zhao, D.G. Truhlar, Acc. Chem. Res. 41 (2008) 157.

[23] J.P. Perdew, K. Burke, M. Ernzerhof, Phys. Rev. Lett. 77 (1996) 3865, Phys. Rev. Lett. (Erratum) 78 (1997) 1386.

[24] B.J. Lynch, P.L. Fast, M. Harris, G.G. Truhlar, J. Phys. Chem. A 104 (2000) 4811.

[25] D. Holschumacher, T. Bannenberg, C.G. Hrib, P.G. Jones, M. Tamm, Angew. Chem. Int. Ed. 47 (2008) 7428.

[26] V. Sumerin, F. Schulz, M. Atsumi, M. Wang, C. Wang, M. Nieger, M. Leskela, T. Repo, P. Pyykko, B. Rieger, J. Am. Chem. Soc. 130 (2008) 14117.

[27] Hybrid fuctionals: B3LYP (20% HF exchange), BH&HLYP (50% HF exchange), MPW1K (42.8% HF exchange), MPW1PW91 (25% HF exchange), M05-2X (56% HF exchange), see details in Ref. [22].

[28] (a) C. Fiolhais, F. Nogueira, M. Marques (Eds.), A Primer in Density Functional Theory, Springer-Verlag, 2003;
(b) W. Koch, M.C. Holthausen, A Chemist's Guide to Density Functional Theory, second ed., Wiley–VCH, Weinheim, 2002;
(c) J. Kohanoff, Electronic Structure Calculations for Solids and Molecules: Theory and Computational Methods, Cambridge University Press, 2006.

[29] S.H. Vosko, L. Wilk, M. Nusair, Can. J. Phys. 58 (1980) 1200.

[30] Details could be found in;
(a) R.G. Parr, W. Yang, Density-Functional Theory of Atoms and Molecules, Oxford, New York, 1989;
(b) J.K. Labanowski, in: J.W. Andzelm (Ed.), Density Functional Methods in Chemistry, Springer-Verlag, Berlin, 1991.

[31] (a) A.D. Becke, J. Chem. Phys. 98 (1993) 1372;
(b) J.P. Perdew, M. Ernzerhof, K. Burke, J. Chem. Phys. 105 (1996) 9982.

[32] (a) G.E. Scuseria, V.N. Staroverov, in: E.E. Dykstra, G. Frenking, K.S. Kim, G.E. Scuseria (Eds.), Theory and Application of Computational Chemistry: The First 40 Years, Elsevier, Amsterdam, 2005, pp. 669–724;
(b) J.P. Perdew, A. Ruzsinszky, J. Tao, V.N. Staroverov, G.E. Scuseria, G. Csonka, J. Chem. Phys. 123 (2005) 062201;
(c) C.A. Jiménez-Hoyos, B.G. Janesko, G.E. Scuseria, Phys. Chem. Chem. Phys. 10 (2008) 6621.

[33] (a) M.P. Waller, H. Braun, N. Hojdis, M. Bühl, J. Chem. Theory Comput. 3 (2007) 2234;
(b) M. Bühl, H. Kabrede, J. Chem. Theory Comput. 2 (2006) 1282.

[34] F. Furche, J.P. Perdew, J. Chem. Phys. 124 (2006) 044103.

[35] (a) Y. Zhao, D.G. Truhlar, J. Chem. Phys. 125 (2006) 194101;
(b) Y. Zhao, D.G. Truhlar, Theor. Chem. Acc. 120 (2008) 215.

[36] See Ref. [2d] for the effect of thermochemical corrections on the potential energy barriers and heat of formation in a related system.

[37] Y. Zhao, D.G. Truhlar, J. Chem. Theory. Comput. 3 (2007) 289, and references therein.

[38] Jaguar 6.0, Schrödinger, LLC, Portland, Oregon, 2005;
Jaguar 7.5, Schrödinger, LLC, New York, NY, 2008.

[39] P.J. Hay, W.R. Wadt, J. Chem. Phys. 82 (1985) 299.

[40] (a) W.J. Hehre, R. Ditchfield, J.A. Pople, J. Chem. Phys. 56 (1972) 2257;
(b) M.M. Francl, W.J. Pietro, W.J. Hehre, J.S. Binkley, M.S. Gordon, D.J. Defrees, J.A. Pople, J. Chem. Phys. 77 (1982) 3654;
(c) P.C. Hariharan, J.A. Pople, Theor. Chim. Acta 28 (1973) 213.

[41] F.A. Hamprecht, A.J. Cohen, D.J. Tozer, N.C. Handy, J. Chem. Phys. 109 (1998) 6264.

[42] (a) A.J. Cohen, N.C. Handy, Chem. Phys. Lett. 316 (2000) 160;
(b) A.D. Boese, N.C. Handy, J. Chem. Phys. 114 (2001) 5497.

[43] J.P. Perdew, K. Burke, Y. Wang, Phys. Rev. B 54 (1996) 16533.

[44] Concerning the MPW1PW91 density functional form, see complete reference in supporting information.

[45] (a) S. Sæbø, P. Pulay, Theor. Chim. Acta 69 (1986) 357;
(b) S. Sæbø, P. Pulay, Ann. Rev. Phys. Chem. 44 (1993) 213;
(c) S. Sæbø, W. Tong, P. Pulay, J. Chem. Phys. 98 (1993) 2170;
(d) J.M. Foster, S.F. Boys, Rev. Mod. Phys. 32 (1960) 300.

[46] Regarding the accuracy and computational efficiency of this technique see R.B. Murphy, M.D. Beachy, R.A. Friesner, M.N. Ringnalda, J. Chem. Phys. 103 (1995) 1481.

[47] Y. Zhao, D.G. Truhlar, J Chem. Theory Comput. 1 (2005) 415.

[48] W. Yu, L. Liang, Z. Lin, S. Ling, M. Haranczyk, M. Gutowski, J. Comput. Chem. 30 (2009) 589, and references therein.

[49] M. Lingwood, J.R. Hammond, D.A. Hrovat, J.M. Mayer, W.T. Borden, J. Chem. Theory Comput. 2 (2006) 740.