

## Application of Semiempirical Methods to Transition Metal Complexes: Fast Results but Hard-to-Predict Accuracy.

Yury Minenkov, Dmitry I. Sharapa, and Luigi Cavallo

*J. Chem. Theory Comput.*, **Just Accepted Manuscript** • DOI: 10.1021/acs.jctc.8b00018 • Publication Date (Web): 22 May 2018

Downloaded from <http://pubs.acs.org> on May 29, 2018

### Just Accepted

“Just Accepted” manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides “Just Accepted” as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. “Just Accepted” manuscripts appear in full in PDF format accompanied by an HTML abstract. “Just Accepted” manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). “Just Accepted” is an optional service offered to authors. Therefore, the “Just Accepted” Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the “Just Accepted” Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these “Just Accepted” manuscripts.

# Application of Semiempirical Methods to Transition Metal Complexes: Fast Results but Hard-to-Predict Accuracy.

*Yury Minenkov,\*§,† Dmitry I. Sharapa‡ and Luigi Cavallo\*†*

§ Moscow Institute of Physics and Technology, Institutskiy Pereulok 9, Dolgoprudny, Moscow Region 141700, Russia

†KAUST Catalysis Center (KCC), King Abdullah University of Science and Technology, Thuwal-23955-6900, Saudi Arabia

‡ Chair of Theoretical Chemistry and Interdisciplinary Center for Molecular Materials Friedrich-Alexander-Universität Erlangen-Nürnberg Egerlandstraße3, 91058 Erlangen, Germany

KEYWORDS: Conformational Sampling, Density Functional Theory, Transition Metals, Conformational Energies, Semiempirical Methods.

ABSTRACT.

A series of semiempirical PM6\* and PM7 methods has been tested in reproducing of relative conformational energies of 27 realistic-size complexes of 16 different transition metals (TMs).

1  
2  
3 An analysis of relative energies derived from single-point energy evaluations on density  
4 functional theory (DFT) optimized conformers revealed pronounced deviations between  
5 semiempirical and DFT methods, indicating fundamental difference in potential energy surfaces  
6 (PES). To identify the origin of the deviation, we compared fully optimized PM7 and respective  
7 DFT conformers. For many complexes, differences in PM7 and DFT conformational energies  
8 have been confirmed often manifesting themselves in false coordination of some atoms (H, O) to  
9 TMs and chemical transformations/distortion of coordination center geometry in PM7 structures.  
10 Despite geometry optimization with fixed coordination center geometry leads to some  
11 improvements in conformational energies, the resulting accuracy is still too low to recommend  
12 explored semiempirical methods for out-of-the-box conformational search/sampling: careful  
13 testing is always needed.  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32

### 33 **1. Introduction**

34  
35  
36 Transition metal (TM) complexes bearing large bulky ligands are examples of important  
37 catalysts, both *in vivo* and in the chemical and pharmaceutical industry.<sup>1-5</sup> To better understand  
38 their catalytic activity and physical properties, theoretical modelling of these complexes is today  
39 routinely undertaken and accounts for a significant fraction of the computational resources used  
40 worldwide.<sup>6-11</sup> The complex electronic structure of TM (which is responsible for their catalytic  
41 activity), implies a number of computational challenges for an accurate modelling, such as  
42 relativistic effects, dynamic and static correlation effects, poor scalability of the reliable  
43 theoretical methods, and multiple low-lying electronic states.<sup>8, 12-20</sup> Numerous strategies have  
44 been proposed to overcome these issues, and many instructive results have been obtained.<sup>21-47</sup> An  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 additional important challenge, the strong conformational flexibility of many TM species, has so  
4 far received only limited attention from selected research groups,<sup>48-58</sup> and is to large extent still  
5 an unsolved problem. This leads to known difficulties in the modeling of large TM complexes  
6 containing multiple rotatable bonds.  
7  
8  
9

10  
11  
12 Accurate conformational search and/or sampling have been shown to be relevant for a number  
13 of cases related to molecular modelling. First, these are useful for modelling of chemical  
14 reactivity since a reaction may not arise from the most stable conformation, and conformational  
15 transitions are often required to initiate a chemical reaction. Moreover, as shown by Besora and  
16 co-workers, the errors originated from choosing wrong conformations can alter the calculated  
17 energy profiles by as much as 10 – 20 kcal/mol.<sup>50, 55</sup> Second, reliable conformational sampling is  
18 often required for interpretation of physical experiments, like NMR,<sup>59</sup> gas phase electron  
19 diffraction or dipole-moment experiments,<sup>60</sup> in order to perform a proper Boltzmann averaging  
20 over the conformational space. Third, conformational sampling is sometimes needed for  
21 quantitative structure activity relationship (QSAR) studies aimed at identifying better catalysts or  
22 drug design because molecular descriptors can be sensitive to the conformations, and using only  
23 the most stable conformation might not be sufficient for reliable predictions.<sup>61</sup>  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39

40 To solve these issues and make accurate calculations of conformational flexible systems  
41 possible, a fast and reliable approach to sample the conformational space of the molecule is of  
42 paramount importance. Needless to say, this is a daunting task since the complexity of this  
43 problem is exponential ( $O^N$ ). A systematic conformational search thus implies minimization of  
44 the energy function ca.  $3^N$  times, where  $N$  is the number of rotatable bonds. To get reliable  
45 relative energy estimates for TM complexes, the energy function from sophisticated wave or  
46 density function theory (DFT) should be used. These energy functions, however, are so  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 computationally intensive that only systems with a few dozens of atoms and 3 – 4 rotatable  
4 bonds can be subjected to an exhaustive conformational search. A possible way to solve these  
5 issues is to use computationally inexpensive energy functions.  
6  
7  
8  
9

10 The cheapest in terms of CPU-time approach to treat the transition metal complexes is  
11 represented by the force field (FF) methods.<sup>62-66</sup> In principle, even the standard and very general  
12 out-of-the-box FF methods, such as the universal force field (UFF) approximation, have been  
13 shown to perform reasonably well for conformational sampling of transition metal complexes.<sup>49</sup>  
14 In cases where the UFF method is not sufficiently accurate, a few more FF-based strategies can  
15 be utilized. Thus, careful parameterization of both metal and functional groups can be done prior  
16 to the conformational search.<sup>56, 58, 65-70</sup> However, the FF parameterization is a tedious task  
17 requiring expertise and can be time consuming. Therefore, this approach is not suitable for  
18 routine applications as in molecular screening, where the conformational sampling of thousands  
19 of molecules is required. In any case, parameterization of a FF is probably the most viable option  
20 in case of conformational search on a single transition metal complex with an immutable  
21 coordination sphere, or when large amount of structures has to be sampled. Another FF-related  
22 approach requiring less manual work is to fix the atoms comprising the transition metal  
23 coordination sphere either at their crystallographic or DFT positions, and run the conformational  
24 search on the organic “non-frozen” part of the complex.<sup>50, 55, 57, 71-77</sup> Semiempirical methods<sup>78-81</sup>  
25 represent another out-of-the-box alternative to FF methods, albeit they are computationally more  
26 intensive, and have been successfully applied for decades in many areas of organic<sup>78-79, 81-92</sup> and  
27 to less extent transition metal chemistry.<sup>33, 36, 45, 78-79, 93-115</sup> Thus, PM3(TM) and PM6  
28 semiempirical methods have been successfully used for conformational search on  
29 molybdenum,<sup>53-54</sup> ruthenium,<sup>116</sup> rhenium<sup>49</sup> and technetium<sup>51</sup> systems. However, their accuracy  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

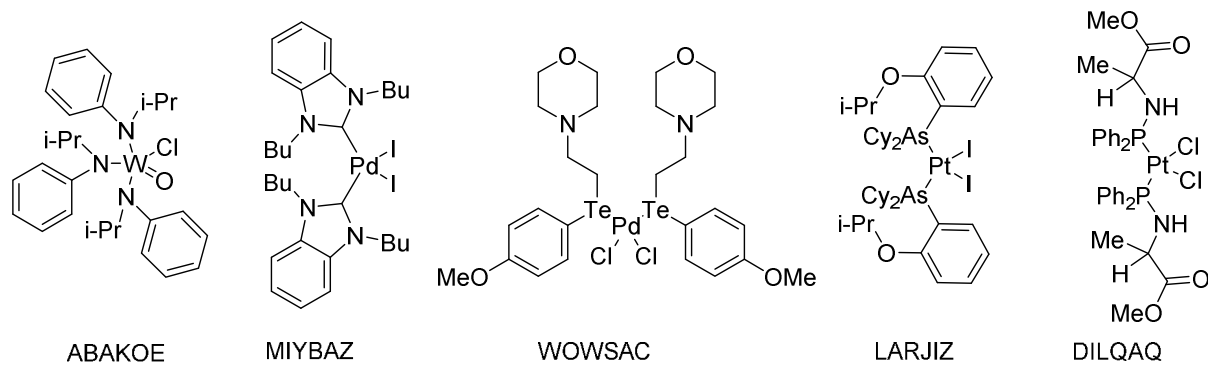
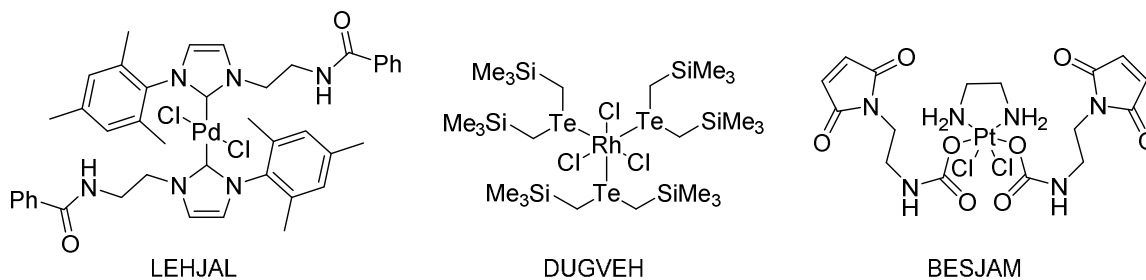
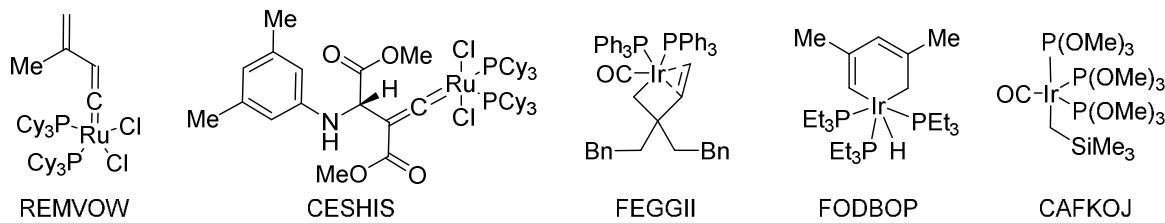
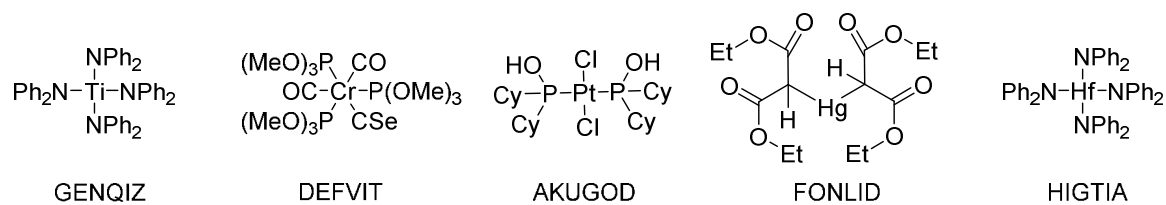
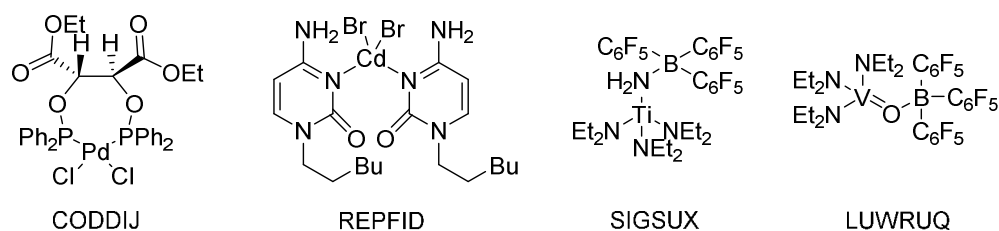
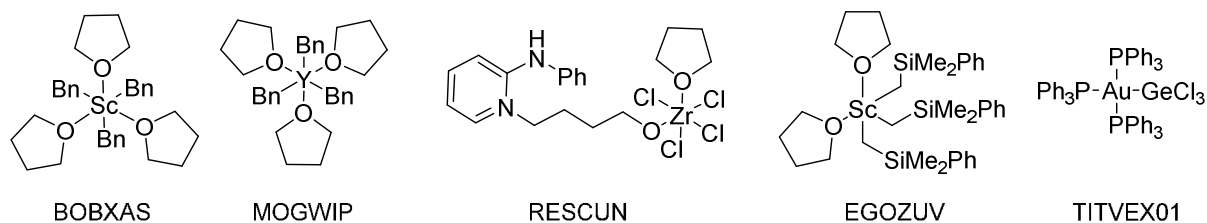
1  
2  
3 for relative conformational energies have never been systematically tested for a series systems  
4 containing various transition metals. In addition, there is no single opinion on the preference of  
5 FF or semiempirical methods for the conformational search of transition metal species.  
6  
7 Comparing FF and semiempirical methods to sample the conformational spaces of a series of  
8 technetium complexes, Buda et al. noted that in a number of cases semiempirical methods are  
9 more reliable than FFs, as the latter could not predict the right isomer.<sup>51</sup> In contrast, Gillespie et  
10 al.<sup>49</sup> showed that a few potential energy minima found during molecular mechanics  
11 conformational search of rhenium complex have disappeared after re-optimization with  
12 semiempirical methods. Taken together these studies indicate that the conformational energy  
13 surface of particular complex apparently depends (sometimes strongly) on the particular method  
14 chosen for geometry optimization, hampering the reliable conformational search.  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27

28 In the current work we seek to contribute to testing an accuracy of semiempirical methods and  
29 generate a database containing 10 very accurate relative conformational energies for each out of  
30 27 realistic sized (ca. 100 atoms) TM complexes initially retrieved from the Cambridge  
31 Structural Database.<sup>117</sup> The developed database was used to test relative conformational energies  
32 from widely available out-of-the-box semiempirical methods: PM6,<sup>112</sup> PM6-D3,<sup>112, 118</sup> PM6-  
33 DH+,<sup>112, 119</sup> PM6-DH2,<sup>112, 120-121</sup> PM6-DH2X,<sup>112, 122</sup> PM6-D3H4,<sup>112, 123</sup> PM6-D3H4X<sup>112, 124</sup> and  
34 PM7<sup>113</sup>. The performance of all methods was carefully analyzed, the most difficult cases were  
35 identified and the origin of the failures discussed in detail.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48

## 49 **2. Computational Details**

### 50 **2.1 Selection of Complexes and Conformer Generation**

1  
2  
3 All the initial structures of the transition metal complexes studied in the present work have been  
4 retrieved from the Cambridge Structural Database (CSD).<sup>117</sup> Pursuing the maximal diversity in  
5  
6 our benchmark set we included complexes of 16 transition metals related to catalysis (Au, Cd,  
7  
8 Cr, Hf, Hg, Ir, Pd, Pt, Rh, Ru, Sc, Ti, V, W, Y, Zr) containing various functional groups and  
9  
10 different covalent and non-covalent ligands. For each complex we have generated 10 conformers  
11  
12 in total from the X-Ray structures as follows. First, the random values of the dihedral angles  
13  
14 corresponding to the rotatable bonds had been set up and the preliminary structure was  
15  
16 generated. Then, to avoid clashing, each structure was pre-optimized with UFF potential by  
17  
18 keeping all the bonds and angle bends at their X-Ray values and relaxing only the dihedral angle  
19  
20 values of the rotatable bonds. All the transition metal complexes studied in this work together  
21  
22 with their CSD names are given in Figure 1.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60





1  
2  
3 **Figure 1.** Transition metal complexes studied in this work together with their Cambridge  
4 Structural Database (CSD) names.  
5  
6  
7

## 8 **2.2 Technical Protocols Utilized to Derive and Compare the Conformational Energies**

9

### 10 **2.2.1 Strategy I**

11

12  
13  
14  
15 In the first part of the study all geometry optimizations of the generated conformers (see Section  
16 2.1) were performed with the local GGA PBE<sup>125-126</sup> functional as implemented in Gaussian 09<sup>127</sup>  
17 suite of programs as this method was found to accurately reproduce the molecular spatial  
18 structures of inorganic species.<sup>34, 128-132</sup> The Grimme's D3(BJ)<sup>118</sup> dispersion correction was  
19 applied to arrive at the PBE-D3(BJ) functional, to account the possible influence of the non-  
20 covalent interaction not covered by standard PBE functional on molecular geometries.<sup>133-135</sup> The  
21 default values were adopted for the self-consistent-field (SCF) and geometry optimization  
22 convergence criteria. Numerical integration of the exchange-correlation (XC) terms was  
23 performed using tighter-than-default "ultrafine" option (pruned, 99 radial shells and 590 angular  
24 points per shell) to eliminate the potential numerical noise in energy second derivatives.  
25 Geometries were characterized as true energy minima by the eigenvalues of the analytically  
26 calculated Hessian matrix.  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43

44 The all-electron double- $\zeta$  basis sets accomplished with single sets of polarization functions  
45 ("def2-svp") of Ahlrichs et al.<sup>136</sup> were used on all the elements with  $Z \leq 36$ . On all the elements  
46 with  $Z > 36$  to account for the scalar relativistic effects the Stuttgart-type effective core  
47 potentials<sup>137</sup> were used to describe the inner (28 electrons on Sn, Cd, Pd, I, Te, Rh, Ru, Y and Zr,  
48 60 electrons on Au, Hf, Hg, Ir, W and Pt) electrons in combination with corresponding def2-svp  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 basis set.<sup>136</sup> The density fitting algorithms with automatic generation of the auxiliary basis sets  
4  
5 were turned on by “Auto” Gaussian 09 keyword to speed up the calculations.  
6  
7

8  
9 The single-point energy evaluations on the structures obtained after geometry optimizations  
10  
11 were performed with the hybrid-meta-GGA M06 functional as implemented in Gaussian 09.  
12  
13 Alike in the geometry optimization procedure, numerical integration of the exchange-correlation  
14  
15 (XC) terms was performed using “ultrafine” grid to eliminate the potential numerical noise in  
16  
17 electronic energy.<sup>138-139</sup> The all-electron triple- $\zeta$  basis sets accomplished with single set of  
18  
19 polarization functions (“def2-tzvp”) of Ahlrichs et al.<sup>136</sup> were used on all the elements with  $Z \leq$   
20  
21 36. On all the elements with  $Z > 36$  to account for the scalar relativistic effects the Stuttgart-type  
22  
23 effective core potentials<sup>137</sup> were used to describe the inner electrons (28 electrons on Sn, Cd, Pd,  
24  
25 I, Te, Rh, Ru, Y and Zr, 60 electrons on Au, Hf, Hg, Ir, Os and Pt) in combination with  
26  
27 corresponding def2-tzvp basis set.<sup>136</sup>  
28  
29  
30  
31

32  
33 Thus obtained conformational energies have been used as references and are denoted as  
34  
35 M06/def2-tzvp//PBE-D3/def2-svp. To show that thus obtained relative conformational energies  
36  
37 are not sensitive to the choice of particular DFT method, we have performed a series of  
38  
39 additional SP energy calculations with PBE0-D3 method and def2-tzvp basis set abbreviated  
40  
41 further as PBE0-D3/def2-tzvp//PBE-D3/def2-svp. In addition, to explore the basis set effect, the  
42  
43 M06/def2-tzvp//PBE-D3/def2-svp relative conformational energies have been systematically  
44  
45 compared with those derived from geometry optimization method, PBE-D3/def2-svp. Notably,  
46  
47 practically in all cases the PBE0-D3/def2-tzvp//PBE-D3/def2-svp and PBE-D3/def2-svp  
48  
49 conformational energies were found to practically mimic their M06/def2-tzvp//PBE-D3/def2-svp  
50  
51 counterparts.  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Finally, the SP energies on the optimized PBE-D3 conformers were calculated with out-of-the-  
4 box semiempirical PM6,<sup>112</sup> PM6-D3,<sup>112, 118</sup> PM6-DH+,<sup>112, 119</sup> PM6-DH2,<sup>112, 120-121</sup> PM6-  
5 DH2X,<sup>112, 122</sup> PM6-D3H4,<sup>112, 123</sup> PM6-D3H4X<sup>112, 124</sup> and PM7<sup>113</sup> methods as implemented in  
6  
7  
8 MOPAC electronic structure package.<sup>140</sup>  
9  
10  
11

## 12 13 **2.2.2 Strategy II**

14  
15  
16 In the second part of the work each structure generated in Section 2.1 and optimized with PBE-  
17 D3/def2-svp protocol as outlined in Section 2.2.1 has been re-optimized with PM7<sup>113</sup>  
18 semiempirical method as implemented in MOPAC electronic structure package.<sup>140</sup> All the  
19 default MOPAC internal values were used apart from the geometry optimization termination  
20 criterion GNORM, for which the default value of 1 kcal·mol<sup>-1</sup>/Å was decreased to 0.1 kcal·mol<sup>-1</sup>  
21 /Å to ensure more precisely optimized structures. The two geometry optimization strategies  
22 were used for optimizing the conformers. In the first strategy, the “non-constrained” geometry  
23 optimization has been performed with the positions of all the atoms relaxed during the  
24 optimization process. In the second strategy, usual for routine conformational search in the  
25 transition metal catalysis, the “constrained” geometry optimization has been performed with  
26 fixed (at their PBE-D3/def2-svp values) positions of transition metal and bonded to transition  
27 metal atoms to preserve the structure of the coordination center. In addition, the positions  
28 (Cartesian coordinates) of few more atoms constituting several functional groups directly bonded  
29 to transition metal were kept fixed in some complexes at their DFT positions as well: GeCl<sub>3</sub>  
30 group in TITVEX01 (Ph<sub>3</sub>P)<sub>3</sub>AuGeCl<sub>3</sub>, CSe group in DEFVIT [(MeO)<sub>3</sub>P]<sub>3</sub>Cr(CO)<sub>2</sub>(CSe), and  
31 CO group in CAFKOJ [(MeO)<sub>3</sub>P]<sub>3</sub>Ir(CO), DEFVIT, FEGGII (-CH<sub>2</sub>-)C(CH<sub>2</sub>OBn)<sub>2</sub>-(CH=CH<sub>2</sub>)-  
32 Ir(PPh<sub>3</sub>)<sub>2</sub>(CO).  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

In both PM7 optimization strategies after the PM7 relative energies for each conformers were derived and tabulated, each conformer was again re-optimized with PBE-D3 method (as in Section 2.2.1) and M06 and PBE0-D3 SP energies with def2-tzvp basis sets were calculated to derive the relative conformational energies as it was done in Section 2.2.1.

## 2.3 Comparing the Conformational Energies

Few quantitative criteria have been used to compare the semiempirical conformational energies with their reference values.

### 2.3.1 Calculation of Pearson Correlation Coefficient

To quantify the correlation between conformational energies from semiempirical computational chemistry methods, PBE0-D3/def2-tzvp//PBE-D3/def2-svp and PBE-D3/def2-svp protocols with reference M06/def2-tzvp//PBE-D3/def2-svp conformational energies, we have calculated the Pearson correlation coefficient ( $\rho$ ) and the squared version thereof ( $\rho^2$ ).

The following formula was used to calculate the Pearson correlation coefficient:

$$\rho(X, Y) = \frac{\sum_{i=1}^n (E_{x,i} - \bar{E}_x)(E_{y,i} - \bar{E}_y)}{\sqrt{\sum_{i=1}^n (E_{x,i} - \bar{E}_x)^2 \sum_{i=1}^n (E_{y,i} - \bar{E}_y)^2}} \quad (1)$$

where X is the tested electronic structure theory method to obtain the conformational energies and Y is the method to obtain the reference conformational energies, i.e. M06/def2-tzvp//PBE0-D3/def2-svp, n is the number of conformations calculated for a given transition metal complex,  $E_i$  is the conformational energy of  $i^{\text{th}}$  conformer, and  $\bar{E}$  is the average conformational energy for n conformers from a given method. The  $\rho$  coefficient can occupy any value in the interval [-1,

1  
2  
3 +1]. If the  $\rho$  value is close to 1 there is an absolute correlation, and if this value is close to -1  
4  
5 there is an anti-correlation.  
6

7  
8 The squared Pearson correlation coefficient ( $\rho^2$ ) is obtained straightforwardly from Eq. 1 and can  
9  
10 be any value in the interval [0, 1]. While the  $\rho^2$  is the most popular criterion in the field of  
11  
12 chemoinformatics to quantitatively measure the correlation ( $\rho^2 \geq 0.95$  indicates excellent  
13  
14 correlation), it can be misleading when describing the quality of the conformational energies  
15  
16 from a certain method as it is always positive and cannot distinguish between correlation and  
17  
18 anti-correlation. In particular, the large (close to 1)  $\rho^2$  values can correspond to both correlation  
19  
20 ( $\rho \approx 1$ ) and anti-correlation ( $\rho \approx -1$ ).  
21  
22  
23  
24  
25

### 26 **2.3.2 Calculation of the Mean Unsigned Deviations in Conformational Energies**

27  
28

29 Another criterion to judge the quality of the relative conformational energies is to calculate the  
30  
31 mean absolute deviation (MUD) between the relative energies obtained with particular method  
32  
33 and corresponding reference values (M06/def-tzvp//PBE-D3/def2-svp). The following formula  
34  
35 was used to calculate the mean absolute deviation of particular complex:  
36  
37  
38

$$39 \text{MUD}(\text{Complex}) = \frac{\sum_{i=0}^n |E_i(X) - E_i(Y)|}{n} \quad (2)$$

40  
41  
42

43 Where X is the tested method, Y is the reference method (M06/def-tzvp//PBE-D3/def2-svp), n is  
44  
45 the number of conformers calculated for the certain complex and  $E_i$  is the relative energy of the  
46  
47 conformer i.  
48  
49  
50

## 51 **3. Results and Discussion**

52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 The results and discussion is organized as follows. First, following the Strategy I, we explored  
4 the potential energy surface (PES) from several electronic structure theory methods. For each  
5 structure/conformer in our dataset we compared the relative conformational energies retrieved  
6 from the semiempirical, PBE-D3/def2-svp, PBE0-D3/def2-tzvp and M06/def2-tzvp SP energies  
7 on the PBE-D3 optimized geometries. Second, following the Strategy II, we estimated the  
8 potential errors arising from the conformational search based on geometry optimization with  
9 semiempirical methods. We performed geometry optimizations with PM7 method of all the  
10 conformers generated in the previous step followed by subsequent PBE-D3/def2-svp geometry  
11 optimizations and PBE0-D3/def2-tzvp and M06/def2-tzvp SP energy evaluations. Finally, the  
12 results are analyzed, the possible origins of the largest deviations are discussed, and conclusions  
13 on the applicability of the semiempirical methods for the conformational search and sampling in  
14 the realistic-size transition metal complexes are given.

### 3.1 Comparing the Relative Conformational Energies Using Strategy I

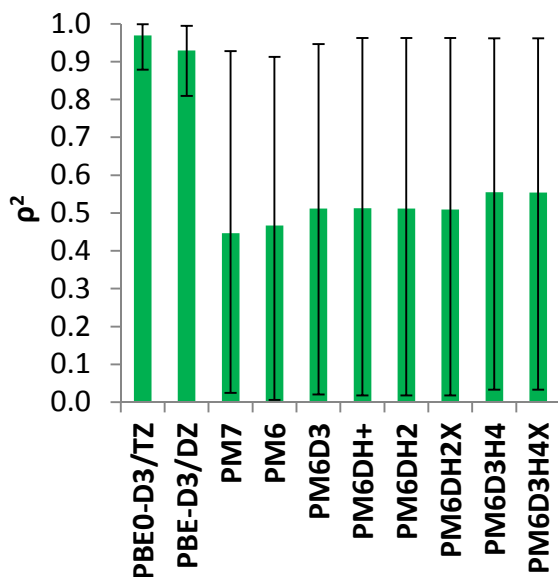
34  
35 The averaged over all the complexes  $\rho^2$  and  $\rho$  (Pearson correlation coefficient) values of  
36 conformational energies derived from the SP energies obtained with all the methods tested on the  
37 PBE-D3/def2-svp geometries with respect to the reference M06/def2-tzvp values are given in  
38 Figures 2 and 3. In addition, the lowest and highest  $\rho^2$  and  $\rho$  values are also given in the Figures  
39 through the solid lines to have an idea of the span.

40  
41  
42 As can be seen from Figure 2, an average PBE0-D3/def2-tzvp and PBE-D3/def2-svp  $\rho^2$  values  
43 turned out to be 0.97 and 0.93, indicating rather strong correlation. Quite large average  $\rho^2$   
44 numbers and an absence of any negative  $\rho$  values for any complex studied in the present work  
45 indicate DFT methods to be quite robust in predicting the relative conformational energies. It  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 suggests the M06/def2-tzvp//PBE-D3/def2-svp protocol to be the reliable source of relative  
4 conformational energies, and we do not expect any significant changes upon change in the  
5 reference SP and geometry optimization method with any other contemporary DFT method  
6  
7  
8  
9  
10 accomplished with the basis set of reasonable quality.

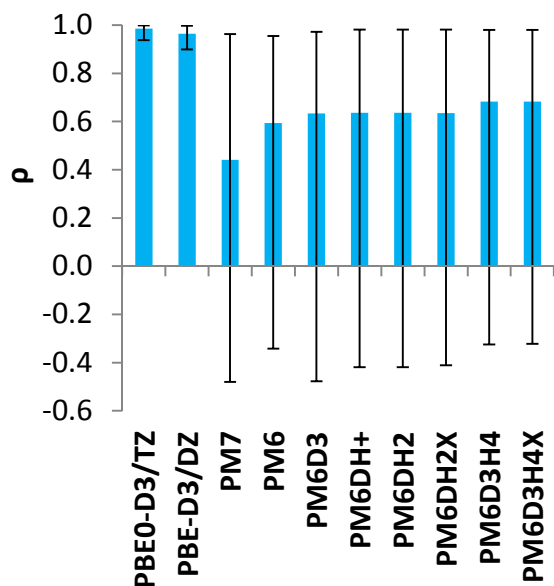
11  
12  
13 Remarkably, for all tested semiempirical methods significantly lower average  $\rho^2$  values all below  
14 0.55 have been obtained. The lowest average values of 0.45 and 0.47 were obtained for PM7 and  
15 PM6 methods, correspondingly. The highest average value of 0.55 were obtained for PM6-D3H4  
16 and PM6-D3H4X methods, indicating only insignificant difference between the best and the  
17 worth performers. The performance of the semiempirical methods is heterogeneous and varies  
18 from complex to complex which is reflected in the large span between the largest and lowest  $\rho^2$   
19 values. Thus, for the most recent PM7 method the smallest  $\rho^2$  value of only 0.02 has been  
20 obtained for DEFVIT complex  $[(\text{MeO})_3\text{P}]_3\text{Cr}(\text{CO})_2(\text{CSe})$  indicating practically no correlation.  
21 Meanwhile, quite high  $\rho^2$  value of 0.93 was obtained for complexes FONLID  $\text{Hg}[\text{CH}(\text{COOEt})_2]_2$   
22 and DUGVEH  $[(\text{Me}_3\text{SiCH}_2)_2\text{Te}]_3\text{RhCl}_3$  which is comparable to DFT performance.

23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37 Another striking difference comparing to the tested DFT methods is existing of negative  $\rho$  values  
38 which, according to Figure 3, have been detected for all the semiempirical methods indicating  
39 signs of anti-correlation in some cases. For example, for PM7 method negative  $\rho$  value was  
40 obtained for 6 out of 27 complexes: TITVEX01  $(\text{Ph}_3\text{P})_3\text{AuGeCl}_3$  ( $\rho=-0.48$ ), CAFKOJ  
41  $[(\text{MeO})_3\text{P}]_3\text{Ir}(\text{CO})$  ( $\rho=-0.42$ ), AKUGOD  $[(\text{Cy})_2\text{P}-\text{OH}]_2\text{PtCl}_2$  ( $\rho=-0.42$ ), BOBXAS  
42  $(\text{Bn})_3\text{Sc}(\text{Furan})_3$  ( $\rho=-0.48$ ), GENQIZ  $\text{Ti}(\text{NPh}_2)_4$  ( $\rho=-0.40$ ) and MOGWIP  $(\text{Bn})_3\text{Y}(\text{Furan})_3$  ( $\rho=-$   
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
0.18).



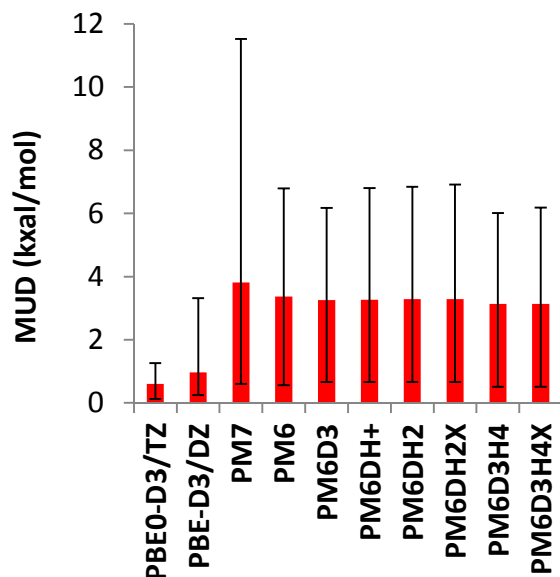
**Figure 2.** The  $\rho^2$  (the squared Pearson correlation coefficient) values obtained for correlation between single-point (SP) energy-based DFT (PBE0-D3/def2-tzvp and PBE-D3/def2-svp) and semiempirical (PM6, PM6-D3, PM6-DH+, PM6-DH2, PM6-DH2X, PM6-D3H4, PM6-D3H4X and PM7) relative conformational energies and their corresponding references (M06/def2-tzvp) for transition metal complexes studied in the present work. The solid bars indicate the average values, and the ends of the solid lines at each bar give the lowest and the highest values.





**Figure 3.** The  $\rho$  (the Pearson correlation coefficient) values obtained for correlation between single-point (SP) energy-based DFT (PBE0-D3/def2-tzvp and PBE-D3/def2-svp) and semiempirical (PM6, PM6-D3, PM6-DH+, PM6-DH2, PM6-DH2X, PM6-D3H4, PM6-D3H4X and PM7) relative conformational energies and their corresponding references (M06/def2-tzvp) for transition metal complexes studied in the present work. The solid bars indicate the average values, and the ends of the solid lines at each bar give the lowest and the highest values.

To explore the quality of the absolute values of the relative conformational energies important for reliable Boltzmann distribution, for each complex we calculated the mean absolute deviations (MUDs) between conformational energies obtained with tested method and their reference (M06/def2-tzvp) counterparts. The results are summarized in Figure 4.



**Figure 4.** The mean unsigned deviation (MUD) values obtained between reference M06/def2-tzvp reference conformational energies and their PBE0-D3/def2-tzvp, PBE-D3/def2-svp, semiempirical (PM6, PM6-D3, PM6-DH+, PM6-DH2, PM6-DH2X, PM6-D3H4, PM6-D3H4X and PM7) counterparts for transition metal complexes studied in the present work. The solid bars indicate the average MUD values, and the ends of the solid lines at each bar give the lowest and the highest MUD values obtained for particular complexes.

For the PBE0-D3/def2-tzvp method the average MUD turned out to be 0.6 kcal/mol. The PBE-D3/def2-svp method with an average MUD of 1.0 kcal/mol is only slightly less accurate. Significantly larger MUDs in range 3.1 (PM6-D3H4 and PM6-D3H4X) to 3.8 (PM7) kcal/mol have been obtained for semiempirical methods. Comparing to DFT methods, notably larger variations in MUD values have been obtained from complex to complex. Thus, the largest PM7 MUD of 11.5 kcal/mol was obtained for CAFKOJ complex  $[(\text{MeO})_3\text{P}]_3\text{Ir}(\text{CO})$  and the lowest MUD of 0.6 kcal/mol was obtained for FONLID complex  $\text{Hg}[\text{CH}(\text{COOEt})_2]_2$ . Combined with respective  $\rho^2$  and  $\rho$  tests, the results indicate quite heterogeneous performance in reproducing of

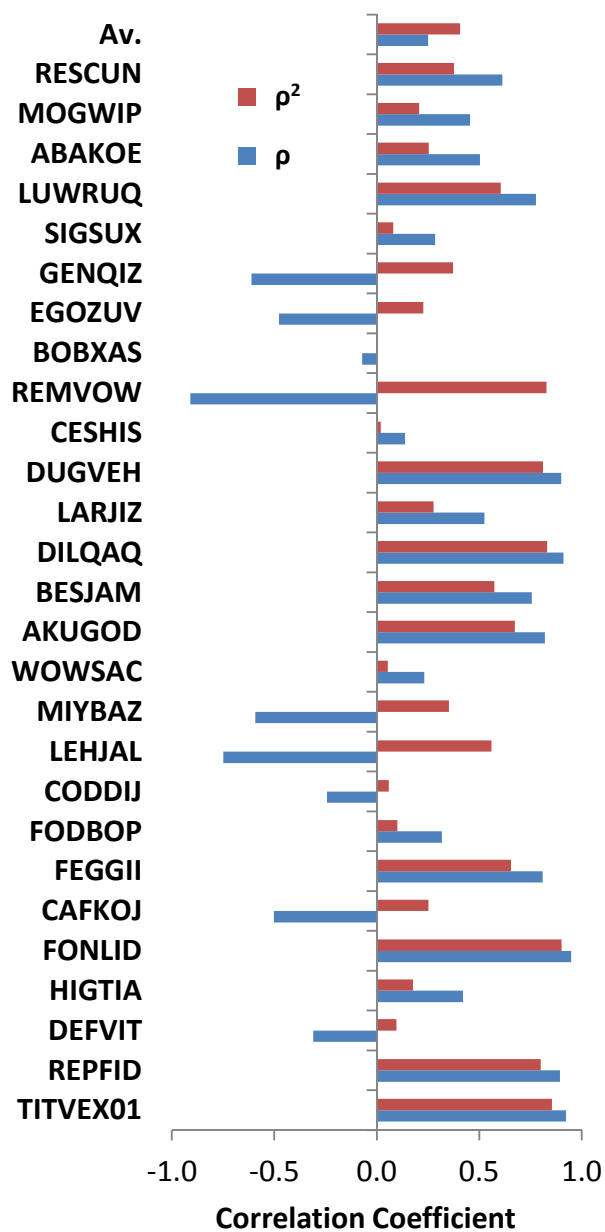
1  
2  
3 the reference conformational energies: good performance for some complexes alternates with  
4  
5 spectacular failures for others.<sup>52</sup>  
6  
7

### 8 9 **3.2 Comparing the Relative Conformational Energies Using Strategy II**

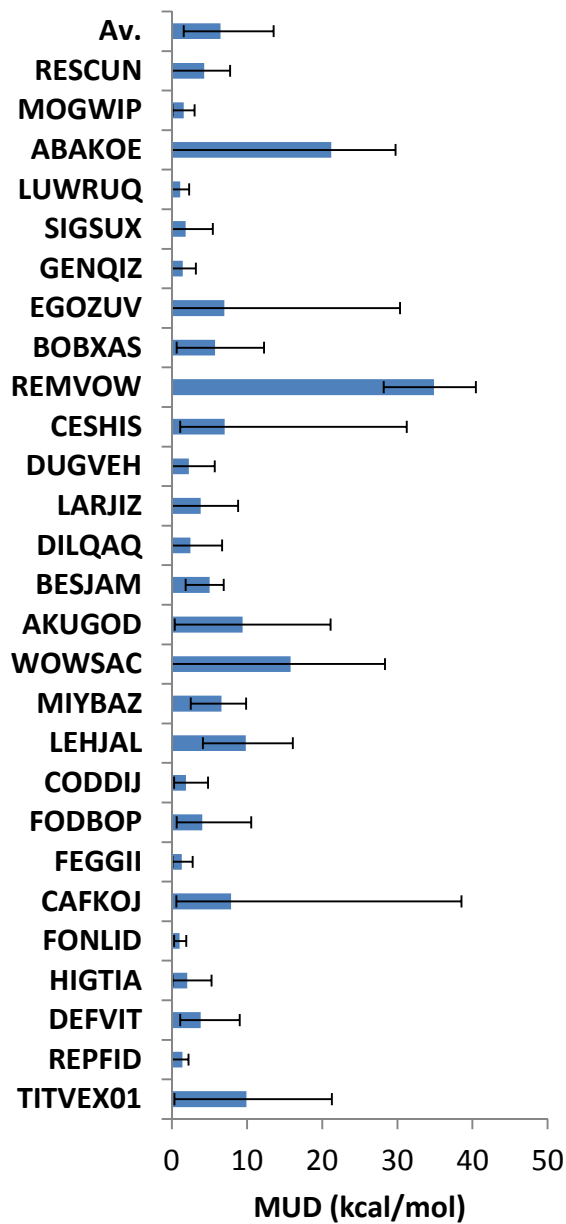
10  
11 Since the semiempirical methods sometimes fail to reproduce the coordination center of  
12 transition metal complexes even qualitatively, we performed the PM7 geometry optimizations in  
13  
14 the two ways: with relaxation of all parameters (unconstrained geometry optimization) and with  
15  
16 fixed atomic positions of the coordination center atoms, see Computational details section 2.2.2.  
17  
18  
19  
20  
21

#### 22 **3.2.1 Unconstrained Geometry Optimization**

23  
24  
25 The  $\rho^2$  and  $\rho$  values between PM7//PM7 and M06-def2-tzvp//PBE-D3/def2-svp relative  
26 conformational energies are presented in Figure 5. The average  $\rho^2$  value obtained for all 27  
27 structures turned out to be 0.41 which is reasonably close to PM7  $\rho^2$  value of 0.45 obtained based  
28 exclusively on SP energies. An average  $\rho$  value turned out to be 0.25 which is smaller than that  
29 of 0.44 based on the SP energies. The largest  $\rho^2$  values followed by positive  $\rho$  values have been  
30 detected for TITVEX01  $(\text{Ph}_3\text{P})_3\text{AuGeCl}_3$  ( $\rho^2/\rho=0.85/0.92$ ), REPFID  $(\text{HexylCyt})_2\text{CdBr}_2$   
31 ( $\rho^2/\rho=0.80/0.89$ ), FONLID  $\text{Hg}[\text{CH}(\text{COOEt})_2]_2$  ( $\rho^2/\rho=0.90/0.95$ ), DILQAC  
32  $[\text{MeOC}(\text{O})\text{CH}(\text{Me})\text{NH-PPH}_2]_2\text{PtCl}_2$  ( $\rho^2/\rho=0.83/0.91$ ) and DUGVEH  $[(\text{Me}_3\text{SiCH}_2)_2\text{Te}]_3\text{RhCl}_3$   
33 ( $\rho^2/\rho=0.81/0.90$ ) indicating correlation. In contrast, large  $\rho^2$  value followed by negative  $\rho$  value  
34 was obtained for REMVOW  $[\text{propen-2-yl}]\text{-CH=C=Ru}(\text{PCy}_3)_2\text{Cl}_2$  ( $\rho^2/\rho=0.83/-0.91$ ) indicating  
35 the anti-correlation, and making black-box application of PM7 method for this complex  
36 dangerous.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



**Figure 5.** The  $\rho^2$  and  $\rho$  correlation coefficients obtained between PM7 relative conformational energies on PM7 geometries and M06/def2-tzvp relative conformational energies on PBE-D3/def2-svp optimized geometries with PM7 optimized geometries used as starting point.



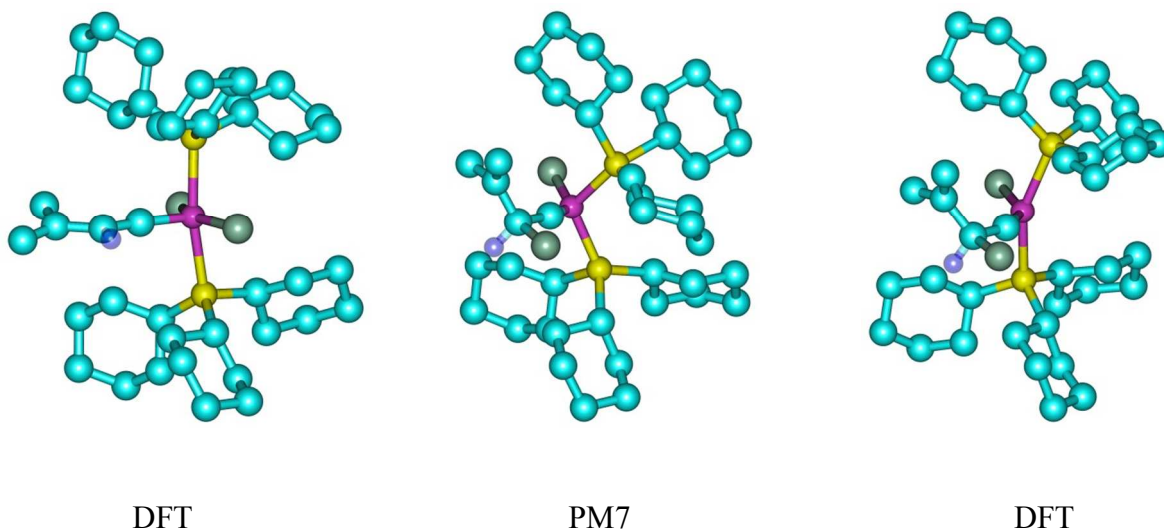
**Figure 6.** The mean unsigned deviation (MUD) values obtained between the PM7//PM7 and M06/def2-tzvp//PBE-D3//def2-svp relative conformational energies for transition metal complexes studied in the present work. The solid bars indicate the average MUD value, and the ends of the solid lines at each bar give the lowest and the highest absolute deviation obtained for particular complexes.

1  
2  
3 In Figure 6 the MUDs obtained between PM7//PM7 and M06/def2-tzvp//PBE-D3/def2-svp  
4 conformational energies are presented for each complex together with the largest and lowest  
5  
6 conformational energies are presented for each complex together with the largest and lowest  
7  
8 absolute deviations in the relative conformational energies. The average MUD turned out to be  
9  
10 6.5 kcal/mol. The lowest MUD of 1.0 kcal/mol has been obtained for complex FONLID  
11  
12 **Hg**[CH(COOEt)<sub>2</sub>]<sub>2</sub> and the largest MUD of 34.9 kcal/mol has been obtained for REMVOW  
13  
14 [propen-2-yl]-CH=C=**Ru**(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>.  
15  
16

17  
18 The manual inspection of all the optimized geometries revealed incorrect PM7 coordination  
19  
20 center geometries of some structures to be responsible for the PM7 failures. One particular  
21  
22 example is conformer 5 of ruthenium complex REMVOW [propen-2-yl]-CH=C=**Ru**(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>.  
23  
24 As depicted in Figure 7, PM7 geometry optimization of this structure resulted in Cl migration  
25  
26 from Ru atom to carbon atom bonded to =C group of ruthenium took place manifesting chemical  
27  
28 transformation. The subsequent PBE-D3/def2-svp optimization did not return Cl atom back to  
29  
30 Ru to lead to initial structure. In contrast to conformer 5, all other conformers of REMVOW did  
31  
32 not undergo to chemical transformation upon PM7 optimization. Similarly, the chemical  
33  
34 transformation occurred upon PM7 geometry optimization of some (or all) conformers turned out  
35  
36 to be responsible for large energy deviations obtained for other complexes, in particular for  
37  
38 TITVEX01 (Ph<sub>3</sub>P)<sub>3</sub>**Au**GeCl<sub>3</sub> (GeCl<sub>3</sub> group dissociation from Au, see Figure S1), FODBOP [-  
39  
40 CH=CMe-CH=CMe-]>**Ir**(H)(PEt<sub>3</sub>)<sub>3</sub> (CH<sub>2</sub> dissociation from Ir for conformer 6, see Figure S2),  
41  
42 LEHJAL [C<sub>21</sub>H<sub>34</sub>N<sub>3</sub>O]<sub>2</sub>**Pd**Cl<sub>2</sub> (coordination of the two hydrogen atoms to Pd, see Figure S3),  
43  
44 MIYBAZ [N,N-diBu-benzimidazoline]<sub>2</sub>**Pd**I<sub>2</sub> (coordination the CH<sub>2</sub> groups to Pd, i.e. change  
45  
46 square planar to octahedral configuration, see Figure S4), WOWSAC [MeOPh-*Te*-(CH<sub>2</sub>)<sub>2</sub>-  
47  
48 Morpholinyl]<sub>2</sub>**Pd**Cl<sub>2</sub> (hydrogen coordination to Pd, see Figure S5), CAFKOJ [(MeO)<sub>3</sub>P]<sub>3</sub>**Ir**(CO)  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

(OMe transfer from P to Ir for conformer 8, see Figure S6), EGOZUV (Furan)<sub>2</sub>Sc(CH<sub>2</sub>SiMe<sub>2</sub>Ph)<sub>3</sub> (dissociation of the two (conformer 2) or one (conformer 5) THF molecules from Sc, Figure S7), CESHIS [C<sub>14</sub>H<sub>17</sub>NO<sub>4</sub>]=C=Ru(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (Cl transfer from Ru to =C group for conformer 9, see Figure S8). At the same time, correctly reproduced coordination center geometry does not guarantee accurate relative conformational energies, as in case of ABAKOE (Ph-*N*-iPr)<sub>3</sub>W(=O)Cl.

An analysis of Figures 5 and 6 combined with manual geometries checks suggests that only for a few (e.g. FONLID Hg[CH(COOEt)<sub>2</sub>]<sub>2</sub>, REPFID (HexylCyt)<sub>2</sub>CdBr<sub>2</sub>, LUWRUQ (Et<sub>2</sub>N)<sub>3</sub>V=O-B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>) out of 27 structures PM7 method can be used to obtain the reliable conformational energies and molecular geometries.



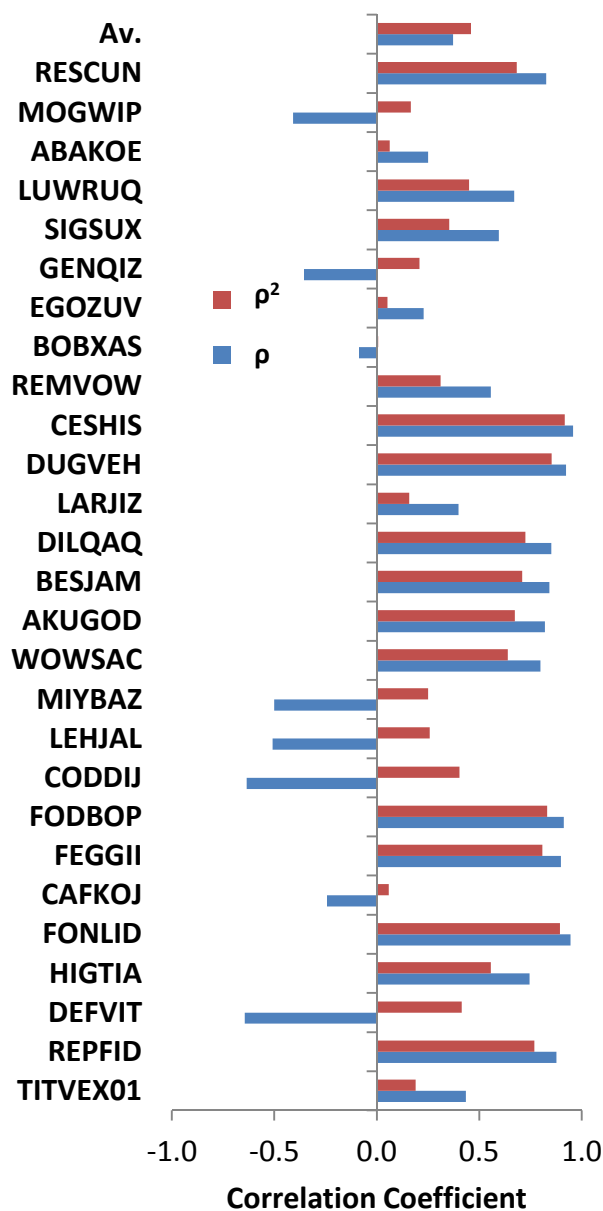
**Figure 7.** The molecular geometries of conformer 5 of REMVOW complex [propen-2-yl]-CH=C=Ru(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>: initial PBE-D3 optimized conformer (left), the same conformer after PM7 geometry optimization (middle), the PM7 structure after subsequent PBE-D3 optimization

(right). Color coding: Ru (Orchid), Cl (Aquamarine), C (Turquoise), P (Orange). Hydrogens of high importance are transparent blue, otherwise - omitted for clarity.

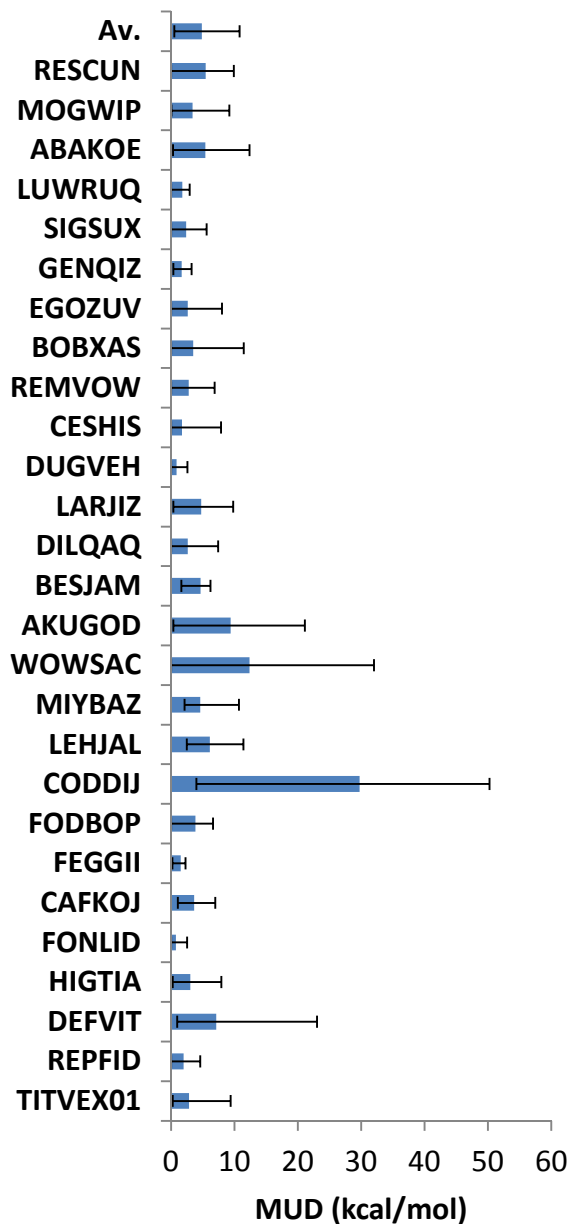
### 3.2.2 Geometry Optimization with Fixed Coordination Center

To see whether the constrained geometry optimization with all the atoms forming coordination center fixed at their DFT positions will improve on PM7 performance, we re-optimized all the PBE-D3 conformers obtained in Part I according to the procedure described in Section 2.2.2. The  $\rho^2$  and  $\rho$  values for correlation between PM7//PM7 and M06/def2-tzvp//PBE-D3/def2-svp relative conformational energies are presented in Figure 8. The average  $\rho^2$  value obtained for all 27 structures turned out to be 0.46 which is practically identical to PM7  $\rho^2$  value of 0.45 obtained based on only SP energies (Part I). An average  $\rho$  value turned out to be 0.37 which is reasonably close to PM7  $\rho$  value of 0.44 based on the SP energies and is higher than PM7  $\rho$  value of 0.25 obtained upon completely unrelaxed PM7 geometry optimizations. The largest  $\rho^2$  values followed by positive  $\rho$  values have been obtained for REPFID (HexylCyt)<sub>2</sub>CdBr<sub>2</sub> ( $\rho^2/\rho=0.77/0.88$ ), FONLID Hg[CH(COOEt)<sub>2</sub>]<sub>2</sub> ( $\rho^2/\rho=0.89/0.95$ ), FEGGII (-CH<sub>2</sub>-)C(CH<sub>2</sub>OBn)<sub>2</sub>-(CH=CH<sub>2</sub>)-Ir(PPh<sub>3</sub>)<sub>2</sub>(CO) ( $\rho^2/\rho=0.81/0.90$ ), FODBOP [-CH=CMe-CH=CMe-]>Ir(H)(PEt<sub>3</sub>)<sub>3</sub> ( $\rho^2/\rho=0.83/0.91$ ), DUGVEH [(Me<sub>3</sub>SiCH<sub>2</sub>)<sub>2</sub>Te]<sub>3</sub>RhCl<sub>3</sub> ( $\rho^2/\rho=0.85/0.92$ ) and CESHIS [C<sub>14</sub>H<sub>17</sub>NO<sub>4</sub>]=C=Ru(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> ( $\rho^2/\rho=0.92/0.961$ ) indicating correlation. No large  $\rho^2$  values followed by negative  $\rho$  values were obtained, indicating certain improvement upon fixed coordination center geometry optimizations.





**Figure 8.** The  $\rho^2$  and  $\rho$  correlation coefficients obtained between PM7 relative conformational energies on PM7 geometries with coordination center fixed during optimization and M06/def2-tzvp relative conformational energies on PBE-D3/def2-svp optimized geometries with PM7 optimized geometries used as starting point.



**Figure 9.** The mean unsigned deviation (MUD) values obtained between the PM7//PM7 (PM7 optimization with coordination center fixed) and M06/def2-tzvp//PBE-D3//def2-svp relative conformational energies for transition metal complexes studied in the present work. The solid bars indicate the average MUD value, and the ends of the solid lines at each bar give the lowest and the highest absolute deviation obtained for particular complexes.

1  
2  
3 In Figure 9 the MUDs obtained between PM7//PME7 (optimization with fixed coordination  
4 center) and M06/def2-tzvp//PBE-D3/def2-svp conformational energies are presented for every  
5 complex together with the largest and lowest absolute deviations in the relative conformational  
6 energies. An average MUD turned out to be 4.9 kcal/mol which is 1.6 kcal/mol lower comparing  
7 to what was obtained for fully relaxed PM7 geometry optimizations in Section 3.2.1. The lowest  
8 MUD of 0.8 kcal/mol has been obtained for complex FONLID  $\text{Hg}[\text{CH}(\text{COOEt})_2]_2$  and the  
9 largest MUD of 29.7 kcal/mol has been obtained for CODDIJ  $\text{DET}(\text{PPh}_2)_2\text{PdCl}_2$ .

10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20 Again the manual inspection of all the geometries has been performed. As all atoms forming the  
21 coordination center have been fixed during PM7 geometry optimization, distorted coordination  
22 center is not an origin of poorly predicted relative conformational energy. However, fixed  
23 coordination sphere does not eliminate another problem revealed for semiempirical methods in  
24 Section 3.2.1: incorrectly predicted coordination of some elements or functional groups to  
25 transition metal. Thus, during the PM7 geometry optimization of CODDIJ  $\text{DET}(\text{PPh}_2)_2\text{PdCl}_2$   
26 an unphysical coordination of one hydrogen atom in conformers 1, 2, 3, 5, 6, 8, 9 (see Figure S9  
27 for conformer 1) or two hydrogen atoms in conformer 7 (see Figure S10) to Pd atom occurred.  
28 As no unphysical hydrogen coordination to Pd observed in conformers 0 and 4, these turned out  
29 to be significantly higher in energy according to PM7. DFT optimization removes false hydrogen  
30 coordination leading to significantly smaller energy diversity in conformational energies of  
31 CODDIJ  $\text{DET}(\text{PPh}_2)_2\text{PdCl}_2$ . Similar unphysical coordination of atoms/functional groups have  
32 also been found in CAFKOJ  $[(\text{MeO})_3\text{P}]_3\text{Ir}(\text{CO})$  (O of O-CH<sub>3</sub> group coordinates to Ir, see Figure  
33 S11), LEHJAL  $[\text{C}_{21}\text{H}_{34}\text{N}_3\text{O}]_2\text{PdCl}_2$  (H of CH<sub>3</sub> groups coordination to Pd, see Figure S12),  
34 MIYBAZ  $[\text{N,N-diBu-benzimidazoline}]_2\text{PdI}_2$  (H of CH<sub>3</sub> coordination to Pd, see Figure S13),  
35 WOWSAC  $[\text{MeOPh-}T_e\text{-(CH}_2)_2\text{-Morpholinyl}]_2\text{PdCl}_2$  (H of CH<sub>2</sub> group coordination to Pd, see  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Figure S14), REMVOW [propen-2-yl]-CH=C=**Ru**(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (H of CH<sub>2</sub> group coordination to  
4  
5 Ru, see Figure S15). Remarkably, large errors have also been obtained for complexes for which  
6  
7 no unphysical coordination to metal atoms occurred, e.g. for ABAKOE (Ph-*N*-iPr)<sub>3</sub>**W**(=O)Cl,  
8  
9 DEFVIT [(MeO)<sub>3</sub>P]<sub>3</sub>**Cr**(CO)<sub>2</sub>(CSe), RESCUN [C<sub>11</sub>H<sub>9</sub>N<sub>2</sub>]-**(CH**<sub>2</sub>)<sub>4</sub>-**O-Zr**(Furan)Cl<sub>4</sub> indicating  
10  
11 fundamental difference between the PES in DFT and semiempirical methods<sup>49</sup> which sometimes  
12  
13 results in a conformational change, see Figures S16-S18.  
14  
15  
16  
17  
18  
19  
20  
21  
22

#### 23 **4. Conclusion**

24  
25  
26 A set of contemporary PM6\*/7 black-box semiempirical methods has been tested to reproduce  
27  
28 the conformational energies of 27 realistic transition metal complexes of 16 transition metals  
29  
30 related to homogeneous catalysis. An analysis of the conformational energies derived from the  
31  
32 single point energy evaluations revealed a pronounced difference between semiempirical and  
33  
34 DFT methods. While conformational energies obtained with DFT protocols perfectly group  
35  
36 together, their PM6\*/7 counterparts turned out to be significantly different for all but a few  
37  
38 complexes. To identify an origin of the deviations, we re-optimized all the conformers with PM7  
39  
40 method followed by DFT optimization mimicking the conformational search procedure in  
41  
42 organometallic chemistry. Comparison of thus obtained PM7-based and DFT-based relative  
43  
44 conformational energies revealed large discrepancies for all but a few complexes, originated  
45  
46 from fundamental differences in PESs often manifesting themselves in chemical  
47  
48 transformations/distortion of coordination center geometry or false coordination of some atoms  
49  
50 (H, O) to transition metals upon PM7 geometry optimization. To minimize these effects, we tried  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 to perform PM7 geometry optimizations with fixed positions of all atoms composing the  
4 coordination sphere. Even if slight improvement in PM7 performance was achieved, still large  
5 discrepancies with DFT conformational energies have survived partly because fixing  
6 coordination center did not prevent false coordination of atoms to transition metal to saturate the  
7 coordination sphere. In cases where no false coordination was observed, an origin of the  
8 difference in conformational energies is the fundamental difference between PESs of DFT and  
9 semiempirical methods. Hence, in general the semiempirical methods are recommended for  
10 conformational search/sampling in transition metal complexes only after careful validation for  
11 particular complex. One possible origin of poor performance of the PM6\*/PM7 semiempirical  
12 methods is related to a limited number of complexes in the MOPAC training set,<sup>141</sup> often  
13 complexes containing necessary diatomic parameters are missing. For example, poor PM7  
14 geometries obtained for TITVEX01 (Ph<sub>3</sub>P)<sub>3</sub>AuGeCl<sub>3</sub> complex might be the result of absence of  
15 reliable Au – Ge diatomic parameters as there are no complexes both containing Au and Ge in  
16 the PM7 training set.<sup>141</sup> Another origin is likely related to the fact that many experimental  
17 formation enthalpies tabulated in numerous databases as NIST webbook<sup>142-143</sup> and utilized to  
18 train semiempirical have been found to be inaccurate.<sup>144-146</sup> We expect that careful re-  
19 parameterization of semiempirical methods will significantly increase their accuracy for  
20 transition metal systems. The obtained database<sup>147</sup> is promising with respect to testing of other  
21 strategies not covered by the present study as ligand field molecular mechanics (LFMM) method  
22 developed by Deeth et al.<sup>67</sup> and available via upcoming Tinker release<sup>68</sup> where additional energy  
23 terms describing the TM center are combined with standard force field terms responsible the  
24 organic part of the molecule, and alternative quantum mechanically derived force field  
25 (QMDF) <sup>148</sup> or tight binding GFN-xTB<sup>36</sup> approaches suggested by Grimme and co-workers.

## ASSOCIATED CONTENT

**Supporting Information.** Cartesian coordinates (Å) of PBE-D3/def2-svp and PM7 optimized structures, M06/def2-tzvp, PBE0-D3/def2-tzvp, PBE-D3/def2-svp, PM6, PM6-D3, PM6-DH+, PM6-DH2, PM6-DH2X, PM6-D3H4, PM6-D3H4X and PM7, tabulated values forming the basis of Figures 2 – 6, Figures 8 – 9 and Figures S1-S18, tabulated conformational energies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## AUTHOR INFORMATION

**Corresponding Author**

\*Yury.Minenkov@mipt.ru

\*Luigi.Cavallo@kaust.edu.sa

## ACKNOWLEDGMENT

We gratefully acknowledge Prof. Frank Jensen, Department of Chemistry, Aarhus University, Denmark, Prof. J. J. P. Stewart, Stewart Computational Chemistry, Colorado Springs, USA and Dr. Alexander M. Genaev, N. N. Vorozhtsov Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia for helpful discussions. The research reported in this publication was supported by funding from King Abdullah University of Science and Technology (KAUST). For computer time, this research used the resources of the Supercomputing Laboratory at King Abdullah University of Science and Technology (KAUST) in Thuwal, Saudi Arabia. Y.M. gratefully acknowledges support from the Government of the Russian Federation (Agreement № 074-02-2018-286).

## REFERENCES

1. Crabtree, R. H., *The Organometallic Chemistry of the Transition Metals*. Wiley: Hoboken, N. J., 2005.
2. Astruc, D., *Organometallic Chemistry and Catalysis*. Springer Berlin Heidelberg: 2007.
3. Grubbs, R. H., *Homogeneous Catalysis : the Applications and Chemistry of Catalysis by Soluble Transition Metal Complexes*. Ed. by Parshall, G.W and Ittel, S. D. Wiley: New York ; Chichester, 1980.
4. Davies, S. G.; Baldwin, J. E., *Organotransition Metal Chemistry: Applications to Organic Synthesis: Applications to Organic Synthesis*. Elsevier Science: Pergamon Press plc, Headington Hill Hall, Oxford OX3 oBW, England, 1982.
5. Ishii, Y.; Tsutsui, M., *Organotransition-Metal Chemistry*. Plenum Press: New York, 1975.
6. Comba, P.; Hambley, T. W.; Martin, B., *Molecular Modeling of Inorganic Compounds*. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2009.
7. Comba, P., *Modeling of Molecular Properties*. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2011.
8. Cramer, C. J.; Truhlar, D. G., Density Functional Theory for Transition Metals and Transition Metal Chemistry. *Phys. Chem. Chem. Phys.* **2009**, *11*, 10757-10816.
9. Lin, Z., Interplay between Theory and Experiment: Computational Organometallic and Transition Metal Chemistry. *Acc. Chem. Res.* **2010**, *43*, 602-611.
10. Frenking, G.; Wagener, T., Transition Metal Chemistry. In *Encyclopedia of Computational Chemistry*, John Wiley & Sons, Ltd: 2002.
11. Bray, M. R.; Deeth, R. J.; Paget, V. J., Kinetics and Mechanism in Transition Metal Chemistry: A Computational Perspective. *Prog. React. Kinet.* **1996**, *21*, 169-214.
12. Cramer, C. J., *Essentials of Computational Chemistry: Theories and Models*. 2nd ed.; Wiley: Chichester, England, 2005.
13. Jensen, F., *Introduction to Computational Chemistry*. 2nd ed.; Wiley: Chichester, England, 2006; p 620.
14. Reiher, M., A Theoretical Challenge: Transition-Metal Compounds. *Chimia* **2009**, *63*, 140-145.
15. Harvey, J. N., On the Accuracy of Density Functional Theory in Transition Metal Chemistry. *Annu. Rep. Prog. Chem., Sect. C: Phys. Chem.* **2006**, *102*, 203-226.
16. Veillard, A., *Quantum Chemistry: The Challenge of Transition Metals and Coordination Chemistry*. Springer Netherlands: 2012.
17. Pierloot, K., Transition Metals Compounds: Outstanding Challenges for Multiconfigurational Methods. *Int. J. Quantum Chem.* **2011**, *111*, 3291-3301.
18. Bencini, A., Some Considerations on the Proper Use of Computational Tools in Transition Metal Chemistry. *Inorg. Chim. Acta* **2008**, *361*, 3820-3831.
19. Davidson, E. R., Computational Transition Metal Chemistry. *Chem. Rev.* **2000**, *100*, 351-352.
20. Bersuker, I. B., *Electronic Structure and Properties of Transition Metal Compounds: Introduction to the Theory*. Wiley: Hoboken, N. J., 2010.
21. Van Eldik, R.; Harvey, J., *Theoretical and Computational Inorganic Chemistry*. Elsevier Science: Academic Press, London, England, 2010; Vol. 62.

- 1  
2  
3 22. Tsipis, A. C., DFT Flavor of Coordination Chemistry. *Coord. Chem. Rev.* **2014**, *272*, 1-  
4 29.  
5 23. Lin, Z. Y., Interplay between Theory and Experiment: Computational Organometallic  
6 and Transition Metal Chemistry. *Acc. Chem. Res.* **2010**, *43*, 602-611.  
7 24. Zhang, X. H.; Chung, L. W.; Wu, Y. D., New Mechanistic Insights on the Selectivity of  
8 Transition-Metal-Catalyzed Organic Reactions: The Role of Computational Chemistry. *Acc.*  
9 *Chem. Res.* **2016**, *49*, 1302-1310.  
10 25. Zein, S.; Neese, F., Ab Initio and Coupled-Perturbed Density Functional Theory  
11 Estimation of Zero-Field Splittings in Mn<sup>II</sup> Transition Metal Complexes. *J. Phys. Chem. A* **2008**,  
12 *112*, 7976-7983.  
13 26. Pantazis, D. A.; Orio, M.; Petrenko, T.; Zein, S.; Bill, E.; Lubitz, W.; Messinger, J.;  
14 Neese, F., A New Quantum Chemical Approach to the Magnetic Properties of Oligonuclear  
15 Transition-Metal Complexes: Application to a Model for the Tetranuclear Manganese Cluster of  
16 Photosystem II. *Chem. - Eur. J.* **2009**, *15*, 5108-5123.  
17 27. Sarmiento-Perez, R.; Botti, S.; Marques, M. A. L., Optimized Exchange and Correlation  
18 Semilocal Functional for the Calculation of Energies of Formation. *J. Chem. Theory Comput.*  
19 **2015**, *11*, 3844-3850.  
20 28. Huntington, L. M. J.; Nooijen, M., Application of Multireference Equation of Motion  
21 Coupled Cluster Theory to Transition Metal Complexes and an Orbital Selection Scheme for the  
22 Efficient Calculation of Excitation Energies. *J. Chem. Phys.* **2015**, *142*, 194111/1-194111/18.  
23 29. Nooijen, M.; Lotrich, V., Extended Similarity Transformed Equation-of-Motion Coupled  
24 Cluster Theory (Extended-STEOM-CC): Applications to Doubly Excited States and Transition  
25 Metal Compounds. *J. Chem. Phys.* **2000**, *113*, 494-507.  
26 30. Comba, P.; Hausberg, S.; Martin, B., Calculation of Exchange Coupling Constants of  
27 Transition Metal Complexes with DFT. *J. Phys. Chem. A* **2009**, *113*, 6751-6755.  
28 31. Tchougreff, A. L.; Soudackov, A. V., Effective Hamiltonian Crystal Fields: Present  
29 Status and Applicability to Magnetic Interactions in Polynuclear Transition Metal Complexes.  
30 *Russ. J. Phys. Chem. A* **2014**, *88*, 1904-1913.  
31 32. Tchougreff, A. L.; Soudackov, A. V.; van Leusen, J.; Koegerler, P.; Becker, K.-D.;  
32 Dronskowski, R., Effective Hamiltonian Crystal Field: Present Status and Applications to Iron  
33 Compounds. *Int. J. Quantum Chem.* **2016**, *116*, 282-294.  
34 33. Sorkin, A.; Truhlar, D. G.; Amin, E. A., Energies, Geometries, and Charge Distributions  
35 of Zn Molecules, Clusters, and Biocenters from Coupled Cluster, Density Functional, and  
36 Neglect of Diatomic Differential Overlap Models. *J. Chem. Theory Comput.* **2009**, *5*, 1254-1265.  
37 34. Bühl, M.; Kabrede, H., Geometries of Transition Metal Complexes from Density  
38 Functional Theory. *J. Chem. Theory Comput.* **2006**, *2*, 1282-1290.  
39 35. Waller, M. P.; Bühl, M., Vibrational Corrections to Geometries of Transition Metal  
40 Complexes from Density Functional Theory. *J. Comput. Chem.* **2007**, *28*, 1531-1537.  
41 36. Grimme, S.; Bannwarth, C.; Shushkov, P., A Robust and Accurate Tight-Binding  
42 Quantum Chemical Method for Structures, Vibrational Frequencies, and Noncovalent  
43 Interactions of Large Molecular Systems Parametrized for All spd-Block Elements ( $Z = 1-86$ ). *J.*  
44 *Chem. Theory Comput.* **2017**, *13*, 1989-2009.  
45 37. Goodpaster, J. D.; Barnes, T. A.; Manby, F. R.; Miller, T. F., III, Density Functional  
46 Theory Embedding for Correlated Wavefunctions: Improved Methods for Open-Shell Systems  
47 and Transition Metal Complexes. *J. Chem. Phys.* **2012**, *137*, 224113/1-224113/10.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



- 1  
2  
3 38. Atanasov, M.; Daul, C. A., Modeling Properties of Molecules with Open d-shells Using  
4 Density Functional Theory. *C. R. Chim.* **2005**, *8*, 1421-1433.
- 5 39. Darkhovskii, M. B.; Chugreev, A. L., Molecular Modeling of Transition-Metal  
6 Complexes with Open d-shell. *Ross. Khim. Zh.* **2004**, *48*, 93-102.
- 7 40. Tchougreeff, A. L.; Darkhovskii, M. B., Molecular Modelling of Metal Complexes with  
8 Open d-shell. *Prog. Theor. Chem. Phys.* **2006**, *15*, 451-505.
- 9 41. Hu, L.; Chen, K.; Chen, H., Modeling  $\sigma$ -Bond Activations by Nickel(0) Beyond  
10 Common Approximations: How Accurately Can We Describe Closed-Shell Oxidative Addition  
11 Reactions Mediated by Low-Valent Late 3d Transition Metal? *J. Chem. Theory Comput.* **2017**,  
12 *13*, 4841-4853.
- 13 42. Craciun, R.; Vincent, A. J.; Shaughnessy, K. H.; Dixon, D. A., Prediction of Reliable  
14 Metal-PH<sub>3</sub> Bond Energies for Ni, Pd, and Pt in the 0 and +2 Oxidation States. *Inorg. Chem.* **2010**,  
15 *49*, 5546-5553.
- 16 43. Manivasagam, S.; Laury, M. L.; Wilson, A. K., Pseudopotential-Based Correlation  
17 Consistent Composite Approach (rp-ccCA) for First- and Second-Row Transition Metal  
18 Thermochemistry. *J. Phys. Chem. A* **2015**, *119*, 6867-6874.
- 19 44. Jiang, W.; DeYonker, N. J.; Determan, J. J.; Wilson, A. K., Toward Accurate Theoretical  
20 Thermochemistry of First Row Transition Metal Complexes. *J. Phys. Chem. A* **2012**, *116*, 870-  
21 885.
- 22 45. Mohr, M.; McNamara, J. P.; Wang, H.; Rajeev, S. A.; Ge, J.; Morgado, C. A.; Hillier, I.  
23 H., The Use of Methods Involving Semi-Empirical Molecular Orbital Theory to Study the  
24 Structure and Reactivity of Transition Metal Complexes. *Faraday Discuss.* **2003**, *124*, 413-428.
- 25 46. Waitt, C.; Ferrara, N. M.; Eshuis, H., Thermochemistry and Geometries for Transition-  
26 Metal Chemistry from the Random Phase Approximation. *J. Chem. Theory Comput.* **2016**, *12*,  
27 5350-5360.
- 28 47. Li, P.; Merz, K. M., Jr., Metal Ion Modeling Using Classical Mechanics. *Chem. Rev.*  
29 **2017**, *117*, 1564-1686.
- 30 48. Fey, N.; Harvey, J. N.; Lloyd-Jones, G. C.; Murray, P.; Orpen, A. G.; Osborne, R.;  
31 Purdie, M., Computational descriptors for chelating P,P- and P,N-donor ligands.  
32 *Organometallics* **2008**, *27*, 1372-1383.
- 33 49. Gillespie, A. M.; Morello, G. R.; White, D. P., De novo ligand design: Understanding  
34 stereoselective olefin binding to  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)]^+$  with molecular mechanics,  
35 semiempirical quantum mechanics, and density functional theory. *Organometallics* **2002**, *21*,  
36 3913-3921.
- 37 50. Balcells, D.; Drudis-Sole, G.; Besora, M.; Dolker, N.; Ujaque, G.; Maseras, F.; Lledos,  
38 A., Some critical issues in the application of quantum mechanics/molecular mechanics methods  
39 to the study of transition metal complexes. *Faraday Discuss.* **2003**, *124*, 429-441.
- 40 51. Buda, C.; Burt, S. K.; Cundari, T. R.; Shenkin, P. S., De novo structural prediction of  
41 transition metal complexes: Application to technetium. *Inorg. Chem.* **2002**, *41*, 2060-2069.
- 42 52. Cundari, T. R., *The Application of Modern Computational Chemistry Methods to*  
43 *Organometallic Systems*. 2007; Vol. 1, p 639-669.
- 44 53. Suarez, D.; Diaz, N.; Lopez, R., A Combined Semiempirical and DFT Computational  
45 Protocol for Studying Bioorganometallic Complexes: Application to Molybdocene-Cysteine  
46 Complexes. *J. Comput. Chem.* **2014**, *35*, 324-334.
- 47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 54. Suarez, D.; Diaz, N., Molecular Modeling of Bioorganometallic Compounds:  
4 Thermodynamic Properties of Molybdocene-Glutathione Complexes and Mechanism of Peptide  
5 Hydrolysis. *Chemphyschem* **2015**, *16*, 1646-1656.
- 6 55. Besora, M.; Braga, A. A. C.; Ujaque, G.; Maseras, F.; Lledos, A., The importance of  
7 conformational search: a test case on the catalytic cycle of the Suzuki-Miyaura cross-coupling.  
8 *Theor. Chem. Acc.* **2011**, *128*, 639-646.
- 9 56. Deeth, R. J., General molecular mechanics method for transition metal carboxylates and  
10 its application to the multiple coordination modes in mono- and dinuclear Mn(II) complexes.  
11 *Inorg. Chem.* **2008**, *47*, 6711-6725.
- 12 57. Drudis-Sole, G.; Ujaque, G.; Maseras, F.; Lledos, A., A QM/MM study of the  
13 asymmetric dihydroxylation of terminal aliphatic n-alkenes with OsO<sub>4</sub>·(DHQD)<sub>2</sub>PYDZ:  
14 Enantioselectivity as a function of chain length. *Chem. Eur. J.* **2005**, *11*, 1017-1029.
- 15 58. Bartol, J.; Comba, P.; Melter, M.; Zimmer, M., Conformational searching of transition  
16 metal compounds. *J. Comput. Chem.* **1999**, *20*, 1549-1558.
- 17 59. Grimme, S.; Bannwarth, C.; Dohm, S.; Hansen, A.; Pisarek, J.; Pracht, P.; Seibert, J.;  
20 Neese, F., Fully Automated Quantum-Chemistry-Based Computation of Spin-Spin-Coupled  
21 Nuclear Magnetic Resonance Spectra. *Angew. Chem. Int. Ed.* **2017**, *56*, 14763-14769.
- 22 60. Vilkov, L. V.; Pentin, Y. A., *Physical Research Methods in Chemistry. Structural*  
23 *Methods and Optical Spectroscopy*. Mir: Moscow, 2003; p 683.
- 24 61. Hechinger, M.; Leonhard, K.; Marquardt, W., What is Wrong with Quantitative  
25 Structure-Property Relations Models Based on Three-Dimensional Descriptors? *J. Chem. Inf.*  
26 *Model.* **2012**, *52*, 1984-1993.
- 27 62. Rappe, A. K.; Casewit, C. J.; Colwell, K. S.; Goddard, W. A.; Skiff, W. M., UFF, a Full  
28 Periodic Table Force Field for Molecular Mechanics and Molecular Dynamics Simulations. *J.*  
29 *Am. Chem. Soc.* **1992**, *114*, 10024-10035.
- 30 63. Rappe, A. K.; Colwell, K. S.; Casewit, C. J., Application of a Universal Force Field to  
31 Metal Complexes. *Inorg. Chem.* **1993**, *32*, 3438-3450.
- 32 64. Comba, P.; Remenyi, R., Inorganic and bioinorganic molecular mechanics modeling - the  
33 problem of the force field parameterization. *Coord. Chem. Rev.* **2003**, *238*, 9-20.
- 34 65. Norrby, P. O.; Brandt, P., Deriving force field parameters for coordination complexes.  
35 *Coord. Chem. Rev.* **2001**, *212*, 79-109.
- 36 66. Hansen, E.; Rosales, A. R.; Tutkowski, B.; Norrby, P. O.; Wiest, O., Prediction of  
37 Stereochemistry using Q2MM. *Acc. Chem. Res.* **2016**, *49*, 996-1005.
- 38 67. Deeth, R. J.; Anastasi, A.; Diedrich, C.; Randell, K., Molecular Modelling for Transition  
39 Metal Complexes: Dealing with d-electron Effects. *Coord. Chem. Rev.* **2009**, *253*, 795-816.
- 40 68. Foscatto, M.; Deeth, R. J.; Jensen, V. R., Integration of Ligand Field Molecular  
41 Mechanics in Tinker. *J. Chem. Inf. Model.* **2015**, *55*, 1282-1290.
- 42 69. Sabolovic, J.; Gomzi, V., Structure Prediction of Bis(amino acidato)copper(II)  
43 Complexes with a New Force Field for Molecular Modeling. *J. Chem. Theory Comput.* **2009**, *5*,  
44 1940-1954.
- 45 70. Tubert-Brohman, I.; Schmid, M.; Meuwly, M., Molecular Mechanics Force Field for  
46 Octahedral Organometallic Compounds with Inclusion of the Trans Influence. *J. Chem. Theory*  
47 *Comput.* **2009**, *5*, 530-539.
- 48 71. Minenkov, Y.; Occhipinti, G.; Jensen, V. R., Metal-Phosphine Bond Strengths of the  
49 Transition Metals: A Challenge for DFT. *J. Phys. Chem. A* **2009**, *113*, 11833-11844.
- 50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 72. Minenkov, Y.; Occhipinti, G.; Heyndrickx, W.; Jensen, V. R., The Nature of the Barrier  
4 to Phosphane Dissociation from Grubbs Olefin Metathesis Catalysts. *Eur. J. Inorg. Chem.* **2012**,  
5 1507-1516.
- 6 73. Feldgus, S.; Landis, C. R., Origin of enantio reversal in the rhodium-catalyzed  
7 asymmetric hydrogenation of prochiral enamides and the effect of the alpha-substituent.  
8 *Organometallics* **2001**, *20*, 2374-2386.
- 9 74. Feldgus, S.; Landis, C. R., Large-scale computational modeling of Rh(DuPHOS) (+)-  
10 catalyzed hydrogenation of prochiral enamides: Reaction pathways and the origin of  
11 enantioselection. *J. Am. Chem. Soc.* **2000**, *122*, 12714-12727.
- 12 75. Landis, C. R.; Feldgus, S., A simple model for the origin of enantioselection and the anti  
13 "lock-and-key" motif in asymmetric hydrogenation of enamides as catalyzed by chiral  
14 diphosphine complexes of Rh(I). *Angew. Chem. Int. Ed.* **2000**, *39*, 2863-2866.
- 15 76. Ujaque, G.; Maseras, F.; Lledos, A., Theoretical characterization of an intermediate for  
16 the [3 + 2] Cycloaddition Mechanism in the Bis(dihydroxy-quinidine)-3,6-Pyridazine-Osmium  
17 Tetroxide-Catalyzed dihydroxylation of styrene. *J. Org. Chem.* **1997**, *62*, 7892-7894.
- 18 77. Ujaque, G.; Maseras, F.; Lledos, A., Theoretical study on the origin of enantioselectivity  
19 in the Bis(dihydroquinidine)-3,6-pyridazine-Osmium Tetroxide-catalyzed dihydroxylation of  
20 styrene. *J. Am. Chem. Soc.* **1999**, *121*, 1317-1323.
- 21 78. Stewart, J. J. P., Semiempirical Molecular Orbital Methods. In *Rev. Comput. Chem.*, John  
22 Wiley & Sons, Inc.: 2007; pp 45-81.
- 23 79. Thiel, W., Semiempirical Quantum-Chemical Methods. *WIREs Comput. Mol. Sci.* **2014**,  
24 *4*, 145-157.
- 25 80. Dewar, M. J. S.; Thiel, W., Ground States of Molecules. 38. MNDO Method -  
26 Approximations and Parameters. *J. Am. Chem. Soc.* **1977**, *99*, 4899-4907.
- 27 81. Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P., The Development and  
28 Use of Quantum Mechanical Molecular Models. 76. AM1 - A New General Purpose Quantum  
29 Mechanical Molecular Model. *J. Am. Chem. Soc.* **1985**, *107*, 3902-3909.
- 30 82. Yilmazer, N. D.; Korth, M., Prospects of Applying Enhanced Semi-Empirical QM  
31 Methods for Virtual Drug Design. *Current Medicinal Chemistry* **2016**, *23*, 2101-2111.
- 32 83. Yilmazer, N. D.; Korth, M., Enhanced semiempirical QM methods for biomolecular  
33 interactions. *Computational and Structural Biotechnology Journal* **2015**, *13*, 169-175.
- 34 84. Rocha, G. B.; Freire, R. O.; Simas, A. M.; Stewart, J. J. P., RM1: A reparameterization of  
35 AM1 for H, C, N, O, P, S, F, Cl, Br, and I. *J. Comput. Chem.* **2006**, *27*, 1101-1111.
- 36 85. Stewart, J. J. P., Optimization of Parameters for Semiempirical Methods. 1. Method. *J.*  
37 *Comput. Chem.* **1989**, *10*, 209-220.
- 38 86. Stewart, J. J. P., Optimization of Parameters for Semiempirical Methods. 2. Applications.  
39 *J. Comput. Chem.* **1989**, *10*, 221-264.
- 40 87. Stewart, J. J. P., Optimization of Parameters for Semiempirical Methods. 3. Extension of  
41 PM3 to Be, Mg, Zn, Ga, Ge, As, Se, Cd, In, Sn, Sb, Te, Hg, Tl, Pb, and Bi. *J. Comput. Chem.*  
42 **1991**, *12*, 320-341.
- 43 88. Hoffmann, R., An Extended Hückel Theory. I. Hydrocarbons. *J. Chem. Phys.* **1963**, *39*,  
44 1397.
- 45 89. Pariser, R.; Parr, R. G., A Semi-Empirical Theory of the Electronic Spectra and  
46 Electronic Structure of Complex Unsaturated Molecules. 1. *J. Chem. Phys.* **1953**, *21*, 466-471.
- 47 90. Pariser, R.; Parr, R. G., A Semi-Empirical Theory of the Electronic Spectra and  
48 Electronic Structure of Complex Unsaturated Molecules. 2. *J. Chem. Phys.* **1953**, *21*, 767-776.
- 49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1
- 2
- 3
- 4 91. Pople, J. A., Electron Interaction in Unsaturated Hydrocarbons. *J. Chem. Soc. Faraday*
- 5 *Trans.* **1953**, *49*, 1375-1385.
- 6 92. Stewart, J. J. P., Special Issue - MOPAC - a Semiempirical Molecular Orbital Program. *J.*
- 7 *Comput. Aided Mol. Des.* **1990**, *4*, 1-45.
- 8 93. Kayi, H.; Clark, T., AM1\* Parameters for Copper and Zinc. *J. Mol. Model.* **2007**, *13*,
- 9 965-979.
- 10 94. Kayi, H.; Clark, T., AM1\* Parameters for Vanadium and Chromium. *J. Mol. Model.*
- 11 **2009**, *15*, 1253-1269.
- 12 95. Kayi, H.; Clark, T., AM1\* Parameters for Bromine and Iodine. *J. Mol. Model.* **2009**, *15*,
- 13 295-308.
- 14 96. Kayi, H.; Clark, T., AM1\* Parameters for Manganese and Iron. *J. Mol. Model.* **2010**, *16*,
- 15 1109-1126.
- 16 97. Kayi, H.; Clark, T., AM1\* Parameters for Cobalt and Nickel. *J. Mol. Model.* **2010**, *16*,
- 17 29-47.
- 18 98. Kayi, H.; Clark, T., AM1\* Parameters for Palladium and Silver. *J. Mol. Model.* **2011**, *17*,
- 19 2585-2600.
- 20 99. Filatov, M. Y.; Zil'berberg, I. L.; Zhidomirov, G. M., NDDO for Metal Compounds
- 21 (NDDO/MC): A New Semiempirical SCF-MO Method for Transition Metal Complexes. *Int. J.*
- 22 *Quantum Chem.* **1992**, *44*, 565-85.
- 23 100. Zilberberg, I. L.; Zhidomirov, G. M., Semiempirical NDDO/MC Calculations of the
- 24 Excited States of the Chromate Ion. *J. Struct. Chem.* **1999**, *40*, 187-191.
- 25 101. Chugreev, A. L., New Generation of Semiempirical Methods of Molecular Modeling
- 26 Based on the Theory of Group Functions. *J. Struct. Chem.* **2007**, *48*, S32-S54.
- 27 102. Ramírez-Solís, A., On the Performance of Local, Semilocal, and Nonlocal Exchange-
- 28 Correlation Functionals on Transition Metal Molecules. *J. Chem. Phys.* **2007**, *126*, 224105/1-
- 29 224105/12.
- 30 103. Bredow, T.; Geudtner, G.; Jug, K., MSINDO Parameterization for Third-Row Transition
- 31 Metals. *J. Comput. Chem.* **2001**, *22*, 861-887.
- 32 104. Imhof, P.; Noe, F.; Fischer, S.; Smith, J. C., AM1/d Parameters for Magnesium in
- 33 Metalloenzymes. *J. Chem. Theory Comput.* **2006**, *2*, 1050-1056.
- 34 105. Winget, P.; Clark, T., AM1\* Parameters for Aluminum, Silicon, Titanium and
- 35 Zirconium. *J. Mol. Model.* **2005**, *11*, 439-456.
- 36 106. Børve, K. J.; Jensen, V. R.; Karlsen, T.; Stovngeng, J. A.; Swang, O., Evaluation of
- 37 PM3(TM) as a Geometry Generator in Theoretical Studies of Transition Metal-Based Catalysts
- 38 for Polymerizing Olefins. *J. Mol. Model.* **1997**, *3*, 193-202.
- 39 107. Cundari, T. R.; Deng, J., PM3(TM) Analysis of Transition-Metal Complexes. *J. Chem.*
- 40 *Inf. Comput. Sci.* **1999**, *39*, 376-381.
- 41 108. Gorelsky, S. I. In *Semiempirical SCF MO Methods, Electronic Spectra, and*
- 42 *configurational interaction*, Elsevier Ltd.: 2004; pp 467-489.
- 43 109. Praveen, P. A.; Babu, R. R.; Ramamurthi, K., Theoretical and Experimental
- 44 Investigations on Linear and Nonlinear Optical Response of Metal Complexes Doped PMMA
- 45 Films. *Materials Research Express* **2017**, *4*, 025024.
- 46 110. Stewart, J. J. P., An Investigation into the Applicability of the Semiempirical Method
- 47 PM7 for Modeling the Catalytic Mechanism in the Enzyme Chymotrypsin. *J. Mol. Model.* **2017**,
- 48 *23*, 154.
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

- 1  
2  
3 111. Christensen, A. S.; Kubar, T.; Cui, Q.; Elstner, M., Semiempirical Quantum Mechanical  
4 Methods for Noncovalent Interactions for Chemical and Biochemical Applications. *Chem. Rev.*  
5 **2016**, *116*, 5301-5337.  
6  
7 112. Stewart, J. J. P., Optimization of Parameters for Semiempirical Methods V: Modification  
8 of NDDO Approximations and Application to 70 Elements. *J. Mol. Model.* **2007**, *13*, 1173-1213.  
9 113. Stewart, J. J. P., Optimization of Parameters for Semiempirical Methods VI: More  
10 Modifications to the NDDO Approximations and Re-optimization of Parameters. *J. Mol. Model.*  
11 **2013**, *19*, 1-32.  
12 114. Borve, K. J.; Jensen, V. R.; Karlsen, T.; Stovng, J. A.; Swang, O., Evaluation of  
13 PM3(tm) as a geometry generator in theoretical studies of transition-metal-based catalysts for  
14 polymerizing olefins. *J. Mol. Model.* **1997**, *3*, 193-202.  
15 115. Decker, S. A.; Donini, O.; Klobukowski, M., A contribution to the understanding of  
16 carbonyl migration in Mn-2(CO)(10) via the pairwise exchange mechanism. *J. Phys. Chem. A*  
17 **1997**, *101*, 8734-8740.  
18 116. Occhipinti, G.; Bjørsvik, H. R.; Jensen, V. R., Quantitative structure-activity  
19 relationships of ruthenium catalysts for olefin metathesis. *J. Am. Chem. Soc.* **2006**, *128*, 6952-  
20 6964.  
21 117. Groom, C. R.; Bruno, I. J.; Lightfoot, M. P.; Ward, S. C., The Cambridge Structural  
22 Database. *Acta Crystallogr. B* **2016**, *72*, 171-179.  
23 118. Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H., A Consistent and Accurate Ab Initio  
24 Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu.  
25 *J. Chem. Phys.* **2010**, *132*, 154104.  
26 119. Korth, M., Third-Generation Hydrogen-Bonding Corrections for Semiempirical QM  
27 Methods and Force Fields. *J. Chem. Theory Comput.* **2010**, *6*, 3808-3816.  
28 120. Rezac, J.; Fanfrlik, J.; Salahub, D.; Hobza, P., Semiempirical Quantum Chemical PM6  
29 Method Augmented by Dispersion and H-Bonding Correction Terms Reliably Describes Various  
30 Types of Noncovalent Complexes. *J. Chem. Theory Comput.* **2009**, *5*, 1749-1760.  
31 121. Korth, M.; Pitoňák, M.; Řezáč, J.; Hobza, P., A Transferable H-Bonding Correction for  
32 Semiempirical Quantum-Chemical Methods. *J. Chem. Theory Comput.* **2010**, *6*, 344-352.  
33 122. Řezáč, J.; Hobza, P., A Halogen-Bonding Correction for the Semiempirical PM6 Method.  
34 *Chem. Phys. Lett.* **2011**, *506*, 286-289.  
35 123. Řezáč, J.; Hobza, P., Advanced Corrections of Hydrogen Bonding and Dispersion for  
36 Semiempirical Quantum Mechanical Methods. *J. Chem. Theory Comput.* **2012**, *8*, 141-151.  
37 124. Brahmshatriya, P. S.; Dobeš, P.; Fanfrlík, J.; Řezáč, J.; Paruch, K.; Bronowska, A.;  
38 Lepšík, M.; Hobza, P., Quantum Mechanical Scoring: Structural and Energetic Insights into  
39 Cyclin-Dependent Kinase 2 Inhibition by Pyrazolo[1,5-a]pyrimidines. *Current Computer-Aided*  
40 *Drug Design* **2013**, *9*, 118-129.  
41 125. Perdew, J. P.; Burke, K.; Ernzerhof, M., Generalized Gradient Approximation Made  
42 Simple. *Phys. Rev. Lett.* **1996**, *77*, 3865-3868.  
43 126. Perdew, J. P.; Burke, K.; Ernzerhof, M., Generalized Gradient Approximation Made  
44 Simple. *Phys. Rev. Lett.* **1997**, *78*, 1396-1396.  
45 127. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman,  
46 J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li,  
47 X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara,  
48 M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.;  
49 Nakai, H.; Vreven, T.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd,  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Gaussian, Inc.: Wallingford, CT, USA, 2009.
128. Minenkov, Y.; Cavallo, L., Ground-State Gas-Phase Structures of Inorganic Molecules Predicted by Density Functional Theory Methods. *ACS Omega* **2017**, *2*, 8373-8387.
129. Girichev, G. V.; Giricheva, N. I.; Koifman, O. I.; Minenkov, Y. V.; Pogonin, A. E.; Semeikin, A. S.; Shlykov, S. A., Molecular Structure and Bonding in Octamethylporphyrin Tin(II), SnN<sub>4</sub>C<sub>28</sub>H<sub>28</sub>. *Dalton Trans.* **2012**, *41*, 7550-7558.
130. Waller, M. P.; Braun, H.; Hojdis, N.; Bühl, M., Geometries of Second-Row Transition Metal Complexes from Density Functional Theory. *J. Chem. Theory Comput.* **2007**, *3*, 2234-2242.
131. Bühl, M.; Reimann, C.; Pantazis, D. A.; Bredow, T.; Neese, F., Geometries of Third-Row Transition-Metal Complexes from Density Functional Theory. *J. Chem. Theory Comput.* **2008**, *4*, 1449-1459.
132. Rydberg, P.; Olsen, L., The Accuracy of Geometries for Iron Porphyrin Complexes from Density Functional Theory. *J. Phys. Chem. A* **2009**, *113*, 11949-11953.
133. Minenkov, Y.; Singstad, Å.; Occhipinti, G.; Jensen, V. R., The Accuracy of DFT-Optimized Geometries of Functional Transition Metal Compounds: A Validation Study of Catalysts for Olefin Metathesis and Other Reactions in the Homogeneous Phase. *Dalton Trans.* **2012**, *41*, 5526-5541.
134. Hujo, W.; Grimme, S., Performance of Non-Local and Atom-Pairwise Dispersion Corrections to DFT for Structural Parameters of Molecules with Noncovalent Interactions. *J. Chem. Theory Comput.* **2013**, *9*, 308-315.
135. Pandey, K. K.; Patidar, P.; Bariya, P. K.; Patidar, S. K.; Vishwakarma, R., Assessment of Density Functionals and Paucity of Non-Covalent Interactions in Aminoylyne Complexes of Molybdenum and Tungsten [(η<sup>5</sup>-C<sub>5</sub>H<sub>5</sub>)(CO)<sub>2</sub>M≡EN(SiMe<sub>3</sub>)(R)] (E = Si, Ge, Sn, Pb): A Dispersion-Corrected DFT Study. *Dalton Trans.* **2014**, *43*, 9955-9967.
136. Weigend, F.; Ahlrichs, R., Balanced Basis Sets of Split Valence, Triple Zeta Valence and Quadruple Zeta Valence Quality for H to Rn: Design and Assessment of Accuracy. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297-3305.
137. Andrae, D.; Häussermann, U.; Dolg, M.; Stoll, H.; Preuss, H., Energy-Adjusted Abinitio Pseudopotentials for the Second and Third Row Transition Elements. *Theor. Chim. Acta* **1990**, *77*, 123-141.
138. Johnson, E. R.; Becke, A. D.; Sherrill, C. D.; DiLabio, G. A., Oscillations in Meta-Generalized-Gradient Approximation Potential Energy Surfaces for Dispersion-Bound Complexes. *J. Chem. Phys.* **2009**, *131*, 034111.
139. Johnson, E. R.; Mackie, I. D.; DiLabio, G. A., Dispersion Interactions in Density Functional Theory. *J. Phys. Org. Chem.* **2009**, *22*, 1127-1135.
140. Stewart, J. J. P. *MOPAC2016*, Stewart Computational Chemistry, Colorado Springs, CO, USA, <http://openmopac.net>, 2016.
141. Stewart, J. J. P. [http://openmopac.net/PM7\\_accuracy/molecules.html](http://openmopac.net/PM7_accuracy/molecules.html). (accessed 02/12/2016).

- 1  
2  
3 142. Chase, M. W., Jr, NIST-JANAF Thermochemical Tables, Fourth Edition. *J. Phys. Chem. Ref. Data* **1998**, *Monograph 9*, 1-1951.
- 4  
5 143. NIST Chemistry Webbook, NIST Standard Reference Database Number 69, Eds. P.J. Linstrom and W.G. Mallard, National Institute of Standards and Technology, Gaithersburg MD, 20899, <http://webbook.nist.gov>, (retrieved December 27, 2017). .
- 6  
7  
8 144. Minenkov, Y.; Sliznev, V. V.; Cavallo, L., Accurate Gas Phase Formation Enthalpies of Alloys and Refractories Decomposition Products. *Inorg. Chem.* **2017**, *56*, 1386 - 1401.
- 9  
10 145. Thanthiriwatte, K. S.; Vasiliu, M.; Battey, S. R.; Lu, Q.; Peterson, K. A.; Andrews, L.; Dixon, D. A., Gas Phase Properties of MX<sub>2</sub> and MX<sub>4</sub> (X = F, Cl) for M = Group 4, Group 14, Cerium, and Thorium. *J. Phys. Chem. A* **2015**, *119*, 5790-5803.
- 11  
12  
13 146. Vasiliu, M.; Feller, D.; Gole, J. L.; Dixon, D. A., Structures and Heats of Formation of Simple Alkaline Earth Metal Compounds: Fluorides, Chlorides, Oxides, and Hydroxides for Be, Mg, and Ca. *J. Phys. Chem. A* **2010**, *114*, 9349-9358.
- 14  
15  
16 147. Minenkov, Y.; Sharapa, D.; Cavallo, L., Accurate conformational energies of large realistic-size transition metal complexes with bulky ligands. <https://doi.org/10.6084/m9.figshare.c.4041149>. **2018**.
- 17  
18  
19 148. Grimme, S., A General Quantum Mechanically Derived Force Field (QMDF) for Molecules and Condensed Phase Simulations. *J. Chem. Theory Comput.* **2014**, *10*, 4497-4514.
- 20  
21  
22  
23  
24  
25  
26  
27

28 For Table of Contents use only

29  
30  
31

