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Consistent Theoretical Description of 1,3-Dipolar Cycloaddition Reactions

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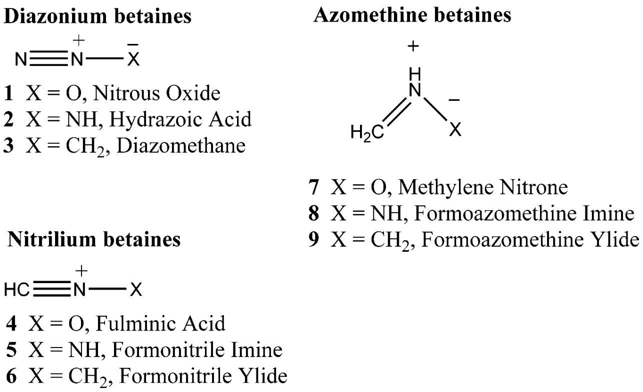
The cycloaddition reactions of 18 1,3-dipolar molecules to ethylene and acetylene have been reinvestigated by quantum chemical methods that are based on a second-order perturbation treatment of electron correlation. It is found that SCS-MP2 and the new perturbative B2-PLYP density functional provide accurate reaction barriers and outperform MP2 as well as standard density functionals such as B3-LYP. The new second-order based methods have the additional advantage that they perform better with increasing quality of the one-particle space, as is desired for a good quantum chemical method. The errors for the reaction enthalpies are in general larger than for the barriers when compared to CBS-QB3 literature values, which is related to strong changes in the electronic structures, but the deviations are again smaller than with MP2 or B3-LYP and are also more systematic. The results of a detailed basis set study suggest that properly polarized triple-ζ AO basis sets represent a good compromise between accuracy and computational speed. The combination of very inaccurate density functionals with small (double-ζ) basis sets, which yields good results for the initial part of the reactions due to error compensation, is not recommended.

There is considerable interest and progress in the development of reliable quantum chemical methods for the prediction of thermochemical and kinetic data of molecules.[1] Modern high-level ab initio quantum chemical calculations are already competitive with experiment for the accurate determination of, e.g., heats of formation and reaction barriers for three to four-atomic systems with up to about 20 electrons (errors <1 kJ·mol^{-1}).[2] More empirical approaches, such as the modern Kohn−Sham density functional theory (KS-DFT), are used to calculate thermochemical and kinetic data of larger molecules of synthetic interest.[3] However, because of the approximate nature of all current density functionals that cannot be improved in a systematic manner, benchmarking on experimental or highly reliable theoretical data is therefore important. This holds particularly for the calculation of reaction barriers as these are often used to distinguish between different mechanisms in chemical reactions.

In this spirit, Ess and Houk (EH)[4] recently presented theoretical activation and reaction enthalpies for various 1,3-dipolar cycloadditions to ethylene and acetylene (see Scheme 1) and a small selection of other pericyclic reactions. They compared MP2,[5] DFT-B3-LYP[6] and DFT-MPW1K[7] results with theoretical reference data at the multicomponent CBS-QB3 level,[8] which is in essence an accurate coupled-cluster method extrapolated to the one-particle basis set limit. Comparison with experimental data for the addition of CH_2N_2 to 1-phenylbutadiene and norbornene gave confidence in the accuracy of the CBS-QB3 method. Although the work of EH goes into the right direction and confirms an earlier more systematic study showing the performance of the DFT method to degrade with larger basis sets,[9] it did not consider the methodological progress of the MP2 method such as SCS-MP2[9] and presents a lopsided view of the DFT-MPW1K method that gives reasonable results only for forward barriers. These aspects and the increased importance of the 1,3-dipolar cycloaddition, particularly the so-called "click" reaction,[10] prompted us to reinvestigate the systems of EH. To allow a direct comparison, we employed their B3-LYP optimized geometries and corrected the energies likewise to enthalpies at 0 K for evaluation against their CBS-QB3 reference values. To investigate the basis set dependence more systematically, we used Dunnings correlation consistent cc-pVXZ AO basis sets (cardinal numbers $X = 2-4$).[11] For the often used a double-ζ type treatment (e.g., $X = 2$ or 6-31G*) significant basis

SCHEME 1: Investigated Dipolar Molecules


Diazonium betaines

1 X = O, Nitrous Oxide
2 X = NH, Hydrazoic Acid
3 X = CH_2, Diazomethane

Nitrilium betaines

4 X = O, Fulminic Acid
5 X = NH, Formonitrile Imine
6 X = CH_2, Formonitrile Ylide

Azomethine betaines

7 X = O, Methylene Nitrone
8 X = NH, Formoazomethine Imine
9 X = CH_2, Formoazomethine Ylide

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set superposition errors can be expected, especially for transition states as well as an unbalanced description of the polar character of the various dipolar molecules. Therefore, to eliminate error compensation, we suggest to use at least $X = 3$ and thus present detailed results only for the cc-pVTZ basis set. Because of the importance to improve quantum chemical methods systematically with the quality of the AO basis, a statistical error-analysis will be also given for $X = 2$ and $X = 4$.

In ref 9 we showed the spin-component-scaled MP2 method (SCS-MP2[12]), which is a logical and physically well-founded correction to MP2, to yield much better reaction energies than MP2. Particularly, the SCS-MP2 and QCISD(T) reaction barriers compare well. As desired for an acceptable quantum chemical method, the SCS-MP2 errors decrease on increasing the basis set, which is not the case for MP2 or B3-LYP. Therefore, SCS-MP2 is preferred over MP2 for main group thermochemistry, also because it is computationally not more demanding. The superior performance of SCS-MP2 is underlined in the present work on the 1,3-dipolar cycloadditions for which EH noted that “the MP2 method gives the expected systematic underestimation of barriers”.

For additional examination of appropriate DFT methods to describe the cycloadditions, we apply a recently developed “fifth-rung” hybrid density functional[13] that includes virtual-orbital dependent terms by second-order type correlation in the spirit of the Görling−Levy Kohn−Sham perturbation theory.[14] For this so-called B2-PLYP functional, the exchange correlation energy is given by

$$E_c = (1 - a_x)\, E_x^{B88} + a_x E_x^{HF} + (1 - c) E_c^{PT2} + c E_c^{LYP}$$

where the second-order perturbational term E_c^{PT2} replaces part of the static and dynamic correlation contributions in the GGA functionals for which the popular B88[15] and LYP[16] forms are used, respectively. The functional contains two global parameters that describe the mixture of HF and GGA exchange ($a_x = 0.53$) and the PT2 and GGA correlation ($c = 0.73$), respectively. According to many realistic tests, B2-PLYP can be regarded as the best general purpose density functional currently available[13] with a mean absolute deviation for the enthalpies of formation in the G2/97 test set[17] of only 1.8 kcal·mol^{-1}, which is smaller than with any other current density functional. Thus, a further aim of our study is to test this “next generation” functional on a well-defined but “hard” problem for the standard methods MP2 and B3-LYP.

The calculated activation ($\Delta H^{\ddagger}$(0K)) and reaction enthalpies ($\Delta_r H$(0K)) for the addition of nine 1,3-dipoles (Scheme 1) to ethylene and acetylene are given in Tables 1 and 2, respectively, as deviations from the CBS-QB3 values of ref 4. Table 3 gives a statistical summary of the performance of all four methods including EH’s data for the MPW1K functional. In addition to mean deviations and mean absolute deviations (MAD), we also suggest the difference of the largest and smallest deviation (error range) as a measure of quality. All calculations were performed with the G03 suite of programs[18] using the cc-pVTZ AO basis set[11] except for the data of Table 4.[5]

The data listed in Table 1 and the statistical analysis in Table 3 convincingly show that SCS-MP2 greatly reduces the MP2 errors for the pericyclic reaction barriers. The systematic underestimation of the barrier heights by MP2 (mean deviation (MD) of −4.5 kcal·mol^{-1}, MAD = 4.5 kcal·mol^{-1}) is almost completely corrected at SCS-MP2 (MD = 0.7, MAD = 1.3, error range = 6.2 kcal·mol^{-1}). Even slightly more accurate is the new second-order hybrid functional B2-PLYP with a similar MAD (1.5 kcal·mol^{-1}) but an even smaller error range (only 2.2 kcal·mol^{-1}). Both approaches, SCS-MP2 and B2-PLYP, outperform B3-LYP (MAD = 3.9 kcal·mol^{-1}) and the MPW1K functional (MAD = 3.2 kcal·mol^{-1}) that has been specially designed for the description of reaction barriers. All DFT approaches tend to overestimate the barriers. A comparison of the errors for the cycloaddition of the same 1,3-dipolar component to ethylene and acetylene shows only minor differences but the description is more consistent for SCS-MP2 and B2-PLYP than for MP2 and B3-LYP.

TABLE 1: Comparison of SCS-MP2, MP2, B2-PLYP and B3-LYP Activation Enthalpies ΔH(0K) Referenced against CBS-QB3 for the 1,3-Dipolar Cycloaddition Reactions of Scheme 1 (in kcal·mol^{-1})

		deviation[a]			
reaction	$\Delta H^{\ddagger}$(0K) CBS-QB3	SCS-MP2	MP2	B2-PLYP	B3-LYP
		Ethylene			
1	27.9	5.0	−0.9	1.3	2.5
2	20.3	3.1	−3.4	1.8	4.0
3	14.6	−0.7	−6.7	2.5	5.7
4	13.0	0.7	−4.5	0.9	3.8
5	7.2	−0.7	−6.3	1.5	4.5
6	5.9	−1.2	−6.8	1.7	5.4
7	13.8	1.1	−4.6	1.4	3.9
8	6.6	−0.6	−6.8	1.6	5.0
9	0.9	0.9	−4.3	2.7	5.6
		Acetylene			
1	28.8	5.0	−0.9	0.9	1.6
2	21.5	3.7	−2.4	1.4	3.0
3	17.3	−0.5	−6.1	2.1	4.5
4	14.6	0.3	−4.8	0.5	3.0
5	9.7	−0.4	−5.6	1.2	3.6
6	8.9	−0.8	−6.0	1.5	4.5
7	15.2	1.6	−3.9	1.2	3.0
8	9.7	0.8	−4.6	1.6	3.7
9	4.0	1.1	−3.4	2.5	4.8

[a] Calculated − reference.

TABLE 2: Comparison of SCS-MP2, MP2, B2-PLYP and B3-LYP Reaction Enthalpies ΔH(0K) Referenced against CBS-QB3 for the 1,3-Dipolar Cycloaddition Reactions of Scheme 1 (in kcal·mol^{-1})

		deviation[a]			
reaction	$\Delta_r H$(0K) CBS-QB3	SCS-MP2	MP2	B2-PLYP	B3-LYP
		Ethylene			
1	−4.4	7.7	7.5	6.8	6.2
2	−19.7	6.1	4.8	7.3	8.6
3	−31.7	2.1	0.2	6.8	10.2
4	−39.3	3.4	3.2	6.3	7.8
5	−57.4	1.1	−0.8	6.7	10.1
6	−68.0	−3.2	−6.4	5.5	11.6
7	−28.8	−1.2	−2.9	4.5	8.5
8	−42.8	−0.2	−2.5	5.2	10.2
9	−62.7	−0.1	−2.4	6.2	12.1
		Acetylene			
1	−37.1	8.1	4.8	4.4	3.3
2	−61.5	6.7	1.6	6.1	6.6
3	−49.0	3.9	1.2	5.8	7.6
4	−74.0	3.9	1.2	4.2	5.0
5	−100.3	2.1	−3.2	5.0	7.4
6	−86.7	−1.2	−5.0	4.5	8.8
7	−43.9	0.7	−0.8	3.2	5.0
8	−60.8	2.0	0.1	3.9	6.0
9	−76.9	2.1	0.6	5.3	8.6

[a] Calculated − reference.

All methods show larger errors for the reaction enthalpies than for the barriers as the electronic (polar) nature of the transition states for the 1,3-dipolar cycloadditions resemble much

TABLE 3: Comparison of Statistical Measures (Mean Deviation, Mean Absolute Deviation, and Error Range) for the Performance of Different Quantum Chemical Methods (in kcal·mol^{-1}) for All 18 Reactions Considered

	mean	MAD	error range[a]
	Reaction Barriers $\Delta H^{\ddagger}$(0K)		
SCS-MP2	0.7	1.3	6.2
MP2	−4.5	4.5	5.9
B2−PYLP	1.5	1.5	2.2
B3-LYP	3.9	3.9	4.1
MPW1K[b]	3.2	3.2	3.4
	Reaction Enthalpies $\Delta_r H$(0K)		
SCS-MP2	2.0	2.7	11.3
MP2	−0.4	2.3	11.2
B2−PLYP	5.1	5.1	4.1
B3-LYP	7.6	7.6	8.8
MPW1K[b]	−12.3	12.3	32.4

[a] Max(deviation) − min(deviation). [b] 6-311+G(2d,p) AO basis from ref 4.

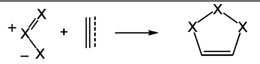
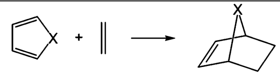
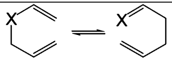
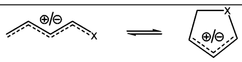
TABLE 4: Mean Absolute Deviations (in kcal·mol^{-1}) for Treatments Employing Correlation Consistent AO Basis Sets cc-pV*X*Z ($X = 2-4$)

	$\Delta H^{\ddagger}$(0K)		$\Delta_r H$(0K)	
	MAD	error range[a]	MAD	error range[a]
		MP2		
cc-pVDZ	4.4	7.0	4.0	17.6
cc-pVTZ	4.5	5.9	2.3	11.2
cc-pVQZ	4.7	5.7	2.6	13.2
		SCS-MP2		
cc-pVDZ	1.5	6.5	3.0	14.4
cc-pVTZ	1.3	6.2	2.7	11.3
cc-pVQZ	1.6	5.9	3.0	11.2
		B3-LYP		
cc-pVDZ	1.7	6.5	2.7	9.9
cc-pVTZ	3.9	4.1	7.6	8.8
cc-pVQZ	4.3	4.3	8.0	8.9
		B2-PLYP		
cc-pVDZ	1.1	4.0	1.6	6.5
cc-pVTZ	1.5	2.2	5.1	4.1
cc-pVQZ	1.5	2.4	5.8	2.7

[a] Max(deviation) − min(deviation).

more the reactants than the products. This is evident from the reference enthalpies that range from only −4.4 kcal·mol^{-1} for the addition of N_2O to ethylene to −100.3 kcal·mol^{-1} for the addition of formonitrile to acetylene. In such difficult situations differences with respect to the basis set limit are about 1−2 kcal·mol^{-1} with the cc-pVTZ basis set (see below) and the error for the CBS-QB3 reference may be also about 1 kcal·mol^{-1}.[19] The data listed in Table 3 show that SCS-MP2 reaction enthalpies do not improve upon those at MP2 as both have almost the same MAD (2.3 and 2.7 kcal·mol^{-1}) and error ranges (11.2 and 11.3 kcal·mol^{-1}). This quite untypical finding[20] is related to the electronic structure of the 1,3-dipoles and was recognized when SCS-MP2 was developed, e.g., for N_2O or HN_3 (reactions 1 and 2).[12] Still, as already noted, on comparing the cycloaddition to ethylene versus those to acetylene SCS-MP2 gives a more consistent description. The B2-PLYP functional yields very systematic deviations from the reference values that are all positive (3.2−7.3 kcal·mol^{-1}), indicating that there is an almost constant shift of the relative energy of multiple versus single bonds. Despite the better MAD values for SCS-MP2 and MP2, the more consistent description of the new B2-PLYP functional is of more chemical value because it follows trends better (error range of only 4.1 kcal·mol^{-1}, MAD = 5.1 kcal·mol^{-1}). Like for the barriers, both second-order approaches outperform B3-LYP (MAD = 7.6, error range = 8.6 kcal·mol^{-1}). The MPW1K functional performs poorest of all with an unacceptable error range exceeding 30 kcal·mol^{-1}!

TABLE 5: Comparison of Statistical Measures (Mean Deviation, Mean Absolute Deviation)[a] for the Performance of Different Quantum Chemical Methods (in kcal·mol^{-1}) for Different Pericyclic Reactions

1,3-Dipolar Cycloadditions[b]			X=CH_2, NH, O,	
	reaction barriers $\Delta H^{\ddagger}$ (0K)[b]		reaction enthalpies $\Delta_r H$(0K)[b]	
	Mean	MAD	Mean	MAD
SCS-MP2	0.7	1.3	2.0	2.7
MP2	-4.5	4.5	-0.4	2.3
B2-PLYP	1.5	1.5	5.1	5.1
B3-LYP	3.9	3.9	7.6	7.6
2+4 (Diels Alder) Cycloadditions[c]			X = none, CH_2, NH, O, SiH_2, PH, S	
	reaction barriers $\Delta H^{\ddagger}$ (0K)		reaction enthalpies $\Delta_r H$(0K)	
	Mean	MAD	Mean	MAD
SCS-MP2	0.2	0.4	0.0	0.6
MP2	-7.7	7.7	-3.7	3.7
B2-PLYP	2.7	2.7	6.8	6.8
B3-LYP	7.8	7.8	13.6	13.6
Cope and Claissen rearrangments[c]			X=CH_2, O,	
	reaction barriers $\Delta H^{\ddagger}$ (0K)		reaction enthalpies $\Delta_r H$(0K)	
	Mean	MAD	Mean	MAD
SCS-MP2	0.2	1.0	2.3	3.8
MP2	-6.4	6.4	2.8	4.2
B2-PLYP	0.4	1.0	-0.9	0.9
B3-LYP	2.3	2.6	-3.2	3.8
Electro cyclisations[c]			X=CH_2, NH,	
	reaction barriers $\Delta H^{\ddagger}$ (0K)		reaction enthalpies $\Delta_r H$(0K)	
	Mean	MAD	Mean	MAD
SCS-MP2	0.1	0.6	-0.1	0.8
MP2	-3.4	3.6	-1.8	1.8
B2-PLYP	1.4	1.9	3.4	3.4
B3-LYP	3.1	3.4	6.1	6.1

[a] Calculated − reference, cc-pVTZ AO basis set. [b] With respect to the CBS-QB3 level of theory. For the 1,3-dipolar molecules X_3, see Scheme 1. [c] With respect to G3 level of theory; see ref 9 for the complete set of reactions.

The basis set dependency of MP2, SCS-MP2, B3-LYP and B2-PLYP is shown in Table 4 by listing MAD values and error ranges as a measure of quality for all 18 instead of individual reactions. The correlation consistent basis sets ranging from double to quadruple-ζ quality ($X = 2-4$) are used. For the barriers, both SCS-MP2 and B2-PLYP behave better with increasing size of the basis set as the MAD is almost constant (i.e., within the error bar of the reference data) and the error range decreases from $X = 2$ to $X = 3$. The changes when using $X = 4$ instead are generally smaller and within the accuracy of the reference data. MP2 and especially B3-LYP perform clearly worse as the MAD increases monotonically from $X = 2$ to $X = 4$. This confirms previous findings for the barriers of other pericyclic reactions.[9] The description of the reaction enthalpies improves for both MP methods with larger basis sets. The significantly smaller error ranges for $X = 3$ compared to $X = 2$ shows once more that double-ζ quality AO basis sets should be avoided for accurate descriptions especially when trends in a series of molecules are of interest. The two DFT methods behave a bit different as the MAD increases with the size of the basis set. However, for B2-PLYP the error level is very small and related to a shift in the enthalpies as can be seen from the monotonic decrease of the error range from $X = 2$ to $X = 4$. Again, B3-LYP performs worst as the MAD increases by about 5 kcal·mol^{-1} when going from $X = 2$ to $X = 3$ with the error range remaining almost constant. The advantage of the expensive cc-pVQZ ($X = 4$) calculation is in general small (and significant only for B2-PLYP) so that cc-pVTZ or similar basis sets appears to be the best compromise between accuracy and computational speed for these methods.

The main result of the present reinvestigation of the 1,3-dipolar cycloadditions to ethylene and acetylene is that second-order perturbation treatments of electron correlation seem to be the most accurate quantum chemical methods for calculating activation and reaction enthalpies of larger systems. This holds both for perturbation theory that is based on Hartree−Fock, but only in the form of the SCS-MP2 method, and for approaches that have their roots in KS-DFT, namely the new B2-PLYP functional. These two methods clearly outperform their popular precursors MP2 and B3-LYP with respect to most statistical performance measures. Our conclusion is underlined by considering also the data for other pericyclic reactions as shown in summary in Table 5 (for details see ref 9) that includes also new B2-PLYP data. The results also demonstrate that special purpose functionals such as MPW1K should be avoided as they are highly unreliable in depicting larger parts of energy surfaces such as product formation in the present study. The nearly nonempirical SCS-MP2 and B2-PLYP methods have the additional advantage that the errors mostly decrease with increasing quality of the one-particle space, as is desired for a good quantum chemical method that should give “the right answer for the right reason”.

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