Benchmarking the Approximate Second-Order Coupled-Cluster Method on Biochromophores

Robert Send,[†] Ville R. I. Kaila,[‡,§,‖] and Dage Sundholm*,[§]

[†]Institut für Physikalische Chemie, Karlsruher Institut für Technologie, Kaiserstrasse 12, 76131 Karlsruhe, Germany

[‡]Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 5 Memorial Drive, Bethesda, Maryland, United States

[§]Department of Chemistry, P.O. Box 55 (A. I. Virtanens plats 1), FIN-00014 University of Helsinki, Finland

[‖]Helsinki Bioenergetics Group, Programme of Structural Biology and Biophysics, Institute of Biotechnology, University of Helsinki, P.O. Box 65, FI-00014 Helsinki, Finland

ABSTRACT: Extensive benchmarking calculations are presented to assess the accuracy of commonly used quantum chemical methods in studying excited state properties of biochromophores. The first few excited states of 12 common model chromophores of photoactive yellow protein, green fluorescent protein, and rhodopsin have been studied using approximate second-order coupled-cluster (CC2) and linear-response time-dependent density functional theory (TDDFT) calculations. The study comprises investigations of basis-set dependences on CC2 excitation energies as well as comparisons of the CC2 results with excitation energies obtained at other computational levels and with experimental data. The basis-set study shows that the accuracy of the two lowest excitation energies is generally sufficient when triple-ζ basis sets augmented with polarization functions are employed, whereas the third and higher excited states were found to require diffuse basis functions in the basis set. Augmenting the basis set with diffuse functions contributes less than 0.15 eV to the excitation energies of low-lying excited states, except for some of the studied anionic states and for Rydberg states. Calculations at the TDDFT level using the B3LYP functional show the necessity of stabilizing anions with point charges or counterions when aiming at reliable electronic excitation spectra. The two lowest excitation energies of the green fluorescent protein and rhodopsin chromophores calculated at the CC2 level agree within 0.15 eV with experimental excitation energies, whereas the B3LYP values are somewhat less accurate, with a maximum deviation of 0.27 eV. The computed excitation energies for the photoactive yellow protein chromophore models deviate from available experimental values by 0.3—0.4 eV and 0.1—0.5 eV, at the CC2 and B3LYP levels of theory, respectively.

■ INTRODUCTION

Prediction of excitation energies is of profound importance in elucidating molecular mechanisms of photochemical and photobiological processes, and in characterizing chemical intermediates determined by spectroscopic techniques. For quantitative predictions, this requires high accuracy of the quantum chemical method, i.e., a deviation of 0.1 eV or less. The use of sufficiently large molecular model systems puts additional constraints on the choice of quantum chemical methods. The accuracy of calculated excitation energies depends on the level of the electron correlation treatment and the basis-set size. Accurate computational approaches such as high-order configuration interaction or coupled-cluster-based methods can yield excitation energies in close agreement with experimental results, provided that the employed basis set is sufficiently large.[1–5] However, such calculations are still limited to very small systems, comprising less than 10 atoms.[6] The use of small basis sets introduces significant errors, implying that the results are unreliable despite the accurate treatment of the electron correlation. Density functional theory (DFT) and low-order *ab initio* electron correlation methods, such as approximate second-order coupled-cluster (CC2) calculations, can be employed in combination with large basis sets to yield results in the complete basis-set limit. However, even the CC2 calculations are computationally very expensive for the larger biochromophores. The linear-response time-dependent DFT (TDDFT) method, which has become a very popular tool for investigating excited states, provides accurate excitation energies at much lower computational cost relative to *ab initio* correlation methods.[7–9] The drawback is a significant number of problematic cases where today's functionals do not provide accurate excitation energies.[2,5,10–13]

Biological chromophores are an intriguing challenge for quantum chemical methods.[14,15] The complexity of biological systems such as protein surroundings are part of these challenges. However, isolated chromophore models of well studied proteins suffice to reveal the limitations of any contemporary excited state quantum chemical method. The discrepancies in the excited state descriptions have caused some controversies but also confusion with respect to the reliability and applicability of the concerned methods.[16–19] There is an increasing amount of extensive experimental gas-phase data for excitation energies of common biological chromophore models.[20–26] These data have been compiled by Ma et al.[27] and used to assess the accuracy of the many-body Green's function approach.[28] The compilation of reference data has revealed the need for benchmarking the most

common excited state methods to obtain an overview of their performance and to resolve the confusion about applicability, basis-set requirements, and further parameter dependencies.

Benchmark sets of vertical excitation energies are numerous, especially for organic chromophores. Most recent efforts comprise the *best estimates* benchmark of the Thiel group, in which reference values are obtained computationally,[10] and the meta studies on various benchmarks by Jacquemin and co-workers.[29] Epifanovsky et al.[30] recently benchmarked excited states of the anionic green fluorescent protein chromophore, which is one of the molecules studied in this work.

Vertical excitation energies are not readily deduced from experimental results. Calculated vertical excitation energies are therefore usually compared to the maxima of the experimental absorption spectra. A more accurate way of benchmarking would be to compare calculated adiabatic excitation energies with experimental results.[31,32] However, such comparisons require information about excited state minima as well as experimentally resolved vibrational spectra, both of which are unavailable for the present series of biochromophores. Thus, we rely on comparisons of vertical excitation energies to experimental absorption maxima and assume that the introduced uncertainties are smaller than the error of the computational method.

In this work, we investigate the basis-set dependence of the lowest excitation energies of important biochromophore models by CC2 calculations with basis sets extended to quadruple-ζ quality. The obtained values are compared to excitation energies and oscillator strengths obtained by TDDFT calculations and to experimental data. The benchmark set comprises seven p-hydroxycinnamic acid chromophore models representing the blue-light photoreceptor of the photoactive yellow protein (PYP), three p-hydroxybenzylideneimidazolinone (pHBDI) chromophore models of the green fluorescent protein (GFP), and two protonated Schiff-base (PSB) retinal models, which are the chromophores of rhodopsin proteins. Part of this study aims at identifying problems in the TDDFT calculations by direct comparison to CC2 results.

This article is structured as follows. The computational methods and the studied chromophores are described in the Computational Details section. The basis-set convergence of the CC2 calculations is discussed in the Results section, where the CC2 and DFT excitation energies obtained in the complete-basis-set limit are also compared to previously calculated and measured values. The main conclusions are summarized in the Conclusions section.

■ COMPUTATIONAL DETAILS

Methods and Basis Sets. This study employs the Karlsruhe basis sets of double-, triple-, and quadruple-ζ quality (def2-SVP, def2-TZVP, and def2-QZVP), as well as the triple-ζ basis set augmented with diffuse functions from Dunning's aug-cc-pVTZ basis set (aug-TZVP).[33−36] The def2 prefix is omitted in the following. The number of spherical (5d, 7f, 9g) basis functions is 2565 in the QZVP calculations on all-*trans*-retinal. Optimization of the molecular ground state structures was performed at the second-order Møller−Plesset perturbation theory (MP2) level employing the TZVP basis sets and the resolution-of-the-identity (RI) approximation.[37−39] The excitation energies were calculated at the CC2 level using the RI approximation.[40−43] The 1s orbitals of C, N, and O were uncorrelated in the *ab initio* calculations. The excitation energies were also calculated at the
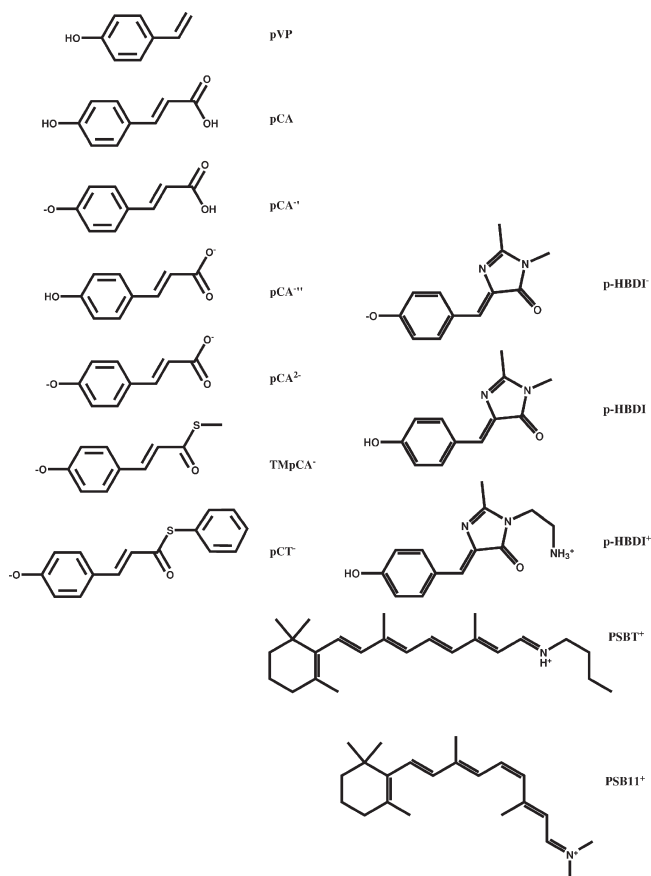

Figure 1. The molecular structures of the studied chromophore models: (a) the photoactive yellow protein chromophore models, (b) the green fluorescent protein chromophore models, (c) the rhodopsin chromophore models.

TDDFT level using Becke's three-parameter functional (B3LYP) and aug-TZVP basis sets.[44−48]

Extrapolated basis-set limits at the CC2 level were estimated by combining values for the excitation energies obtained with the three largest basis sets (TZVP, aug-TZVP, and QZVP). All calculations were done with Turbomole version 6.1[49] on a Linux cluster equipped with 2.6 GHz AMD Opteron processors. The calculations are computationally demanding. Typical computational times for the CC2 calculations are 100 CPU hours for calculating the first excited state of HBDI$^−$ using the QZVP basis set and 150 CPU hours for obtaining the first excited state of PSBT$^+$ at the CC2/TZVP level.

Benchmark Set Composition. In this work, we investigate the biochromophores shown in Figure 1, recently studied by Ma et al. at the many-body Green's function theory (MBGFT) level.[27] The abbreviations reported in the figure indicate the protonation states with prime (phenolate) and double prime (carboxylate) symbols, as well as the total charge of the molecular system. TDDFT calculations on the anionic chromophores are also performed with external point charges to obtain charge neutrality. The point charges ensure that the DFT ionization threshold is larger than the studied excitation energies.

Photoactive Yellow Protein Chromophore Models. The PYP molecule is a bacterial photoreceptor, responsible for absorbing blue light photons by its p-coumaric acid chromophore.[50,51] The studied PYP chromophore models comprise *trans*-p-coumaric acid
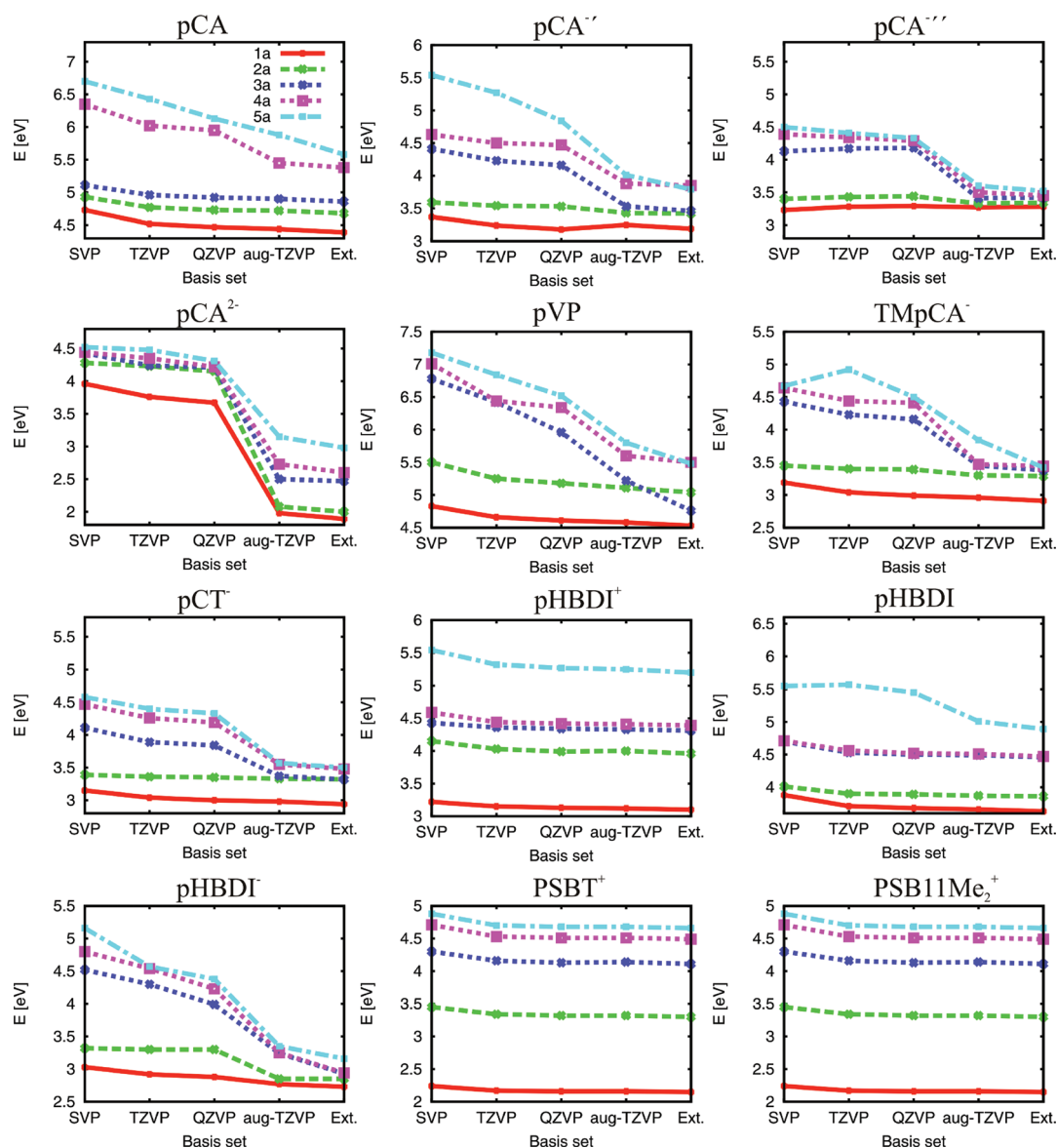
Figure 2. The basis-set convergence of the five lowest singlet excitation energies (in eV) of the investigated chromophore models studied at the CC2 level. The extrapolated aug-QZVP excitation energies are denoted Ext. The legend for the line structures is only given in the first subfigure.

(pCA), deprotonated *trans*-p-coumaric acid (pCA^{-}′), *trans*-p-coumarate (pCA^{-}″), deprotonated *trans*-p-coumarate (pCA^{2-},) p-vinyl phenol (pVP), thiomethyl-p-coumarate (TMpCA^{-}), and thiophenyl p-coumarate (pCT^{-}), shown in Figure 1a.

Green Fluorescent Protein Chromophore Models. The GFP molecule is responsible for the bioluminescence of many marine organisms.[52] The luminescence takes place only when its chromophore, pHBDI embedded in the β-barrel structure of the protein, is exposed to blue light but not in solution.[52] Three GFP model chromophores, shown in Figure 1b, are investigated, namely, pHBDI, pHBDI^{-}, and pHBDI^{+}. The phenol group is deprotoned in the pHBDI^{-} model, and the methyl group of the imidazolinone nitrogen in the pHBDI model is substituted by a protonated ethylamine group ($-CH_2CH_2NH_3^{+}$) in the pHBDI^{+} model.

Rhodopsin Chromophore Models. Rhodopsin is a G-protein coupled receptor, responsible for light absorption in vertebrate visual pigments.[53,54] Two models of the light absorbing

chromophore of rhodopsin were studied, 11-*cis* and all-*trans* retinal (Figure 1c). In the former chromophore model, a butyl group is connected to the protonated nitrogen atom of the retinyl chain, simulating the cross-linked Lys-296 in the protein. In the latter chromophore model, the Schiff base nitrogen has two methyl substituents. Both models have a net positive charge of +1.

■ RESULTS

Basis-Set Convergence of the CC2 Calculations. The basis set convergence of the five lowest singlet excited states is shown in Figure 2 and Tables 1−4. The two lowest excited states of most chromophores are valence states and well described using the TZVP basis sets. The excitation energies obtained at the CC2/TZVP level deviate less than 0.15 eV from the extrapolated CC2/aug-QZVP values. The pHBDI^{-} chromophore constitutes an exception, where the second excited state obtained at the

Table 1. Basis-Set Dependence of the CC2 Excitation Energies (in eV) for the Five Lowest Excited Singlet States of the Photoactive Yellow Protein Chromophore Models pCA, pCA$^{-\prime}$, pCA$^{-\prime\prime}$, and pCA^{2-a}

molecule	basis	1a	2a	3a	4a	5a
pCA	SVP	4.73	4.93	5.11	6.35	6.70
pCA	TZVP	4.52	4.77	4.96	6.02	6.43
pCA	QZVP	4.47	4.73	4.92	5.95	6.13
pCA	aug-TZVP	4.44	4.72	4.90	5.45	5.88
pCA	extrapolated	4.39	4.68	4.86	<u>5.38</u>	<u>5.58</u>
pCA	oscillator strength	0.54	0.27	0.00	0.22	0.16
pCA$^{-\prime}$	SVP	3.37	3.59	4.41	4.63	5.54
pCA$^{-\prime}$	TZVP	3.24	3.54	4.23	4.50	5.27
pCA$^{-\prime}$	QZVP	3.18	3.53	4.16	4.47	4.84
pCA$^{-\prime}$	aug-TZVP	3.25	3.43	3.53	3.88	4.01
pCA$^{-\prime}$	extrapolated	3.19	3.42	<u>3.46</u>	<u>3.85</u>	<u>3.79</u>
pCA$^{-\prime}$	oscillator strength	1.01	0.00	0.10	0.00	0.05
pCA$^{-\prime\prime}$	SVP	3.23	3.40	4.13	4.39	4.50
pCA$^{-\prime\prime}$	TZVP	3.28	3.43	4.17	4.34	4.41
pCA$^{-\prime\prime}$	QZVP	3.29	3.44	4.18	4.29	4.33
pCA$^{-\prime\prime}$	aug-TZVP	3.27	3.33	3.41	3.50	3.60
pCA$^{-\prime\prime}$	extrapolated	3.28	3.34	<u>3.42</u>	<u>3.45</u>	<u>3.52</u>
pCA$^{-\prime\prime}$	oscillator strength	0.00	0.00	0.02	0.02	0.05
pCA^{2-}	SVP	3.96	4.28	4.43	4.44	4.52
pCA^{2-}	TZVP	3.76	4.23	4.24	4.35	4.48
pCA^{2-}	QZVP	3.67	4.15	4.21	4.22	4.31
pCA^{2-}	aug-TZVP	1.98	2.08	2.50	2.73	3.15
pCA^{2-}	extrapolated	<u>1.89</u>	<u>2.00</u>	<u>2.47</u>	<u>2.60</u>	<u>2.98</u>
pCA^{2-}	oscillator strength	0.13	0.04	0.69	0.00	0.00

^{a} The molecular structures were optimized for the ground state at the MP2/TZVP level. Excitation energies for Rydberg and anionic states that demand diffuse basis functions in the basis set are underlined. The oscillator strengths calculated at the CC2/TZVP level are given.

Table 2. Basis-Set Dependence of the CC2 Excitation Energies (in eV) for the Five Lowest Excited Singlet States of the Photoactive Yellow Protein Chromophore Models pVP, TMpCA$^-$, and pCT^{-a}

molecule	basis	1a	2a	3a	4a	5a
pVP	SVP	4.83	5.50	6.78	7.01	7.18
pVP	TZVP	4.66	5.25	6.42	6.44	6.84
pVP	QZVP	4.61	5.18	5.96	6.34	6.52
pVP	aug-TZVP	4.58	5.11	5.22	5.60	5.80
pVP	extrapolated	4.53	5.04	<u>4.76</u>	<u>5.50</u>	<u>5.48</u>
pVP	oscillator strength	0.05	0.52	0.00	0.28	0.45
TMpCA$^-$	SVP	3.19	3.45	4.43	4.64	4.67
TMpCA$^-$	TZVP	3.04	3.40	4.23	4.44	4.92
TMpCA$^-$	QZVP	2.99	3.39	4.16	4.41	4.50
TMpCA$^-$	aug-TZVP	2.96	3.30	3.45	3.47	3.84
TMpCA$^-$	extrapolated	2.91	3.29	<u>3.38</u>	<u>3.44</u>	<u>3.42</u>
TMpCA$^-$	oscillator strength	1.21	0.00	0.09	0.00	0.00
pCT$^-$	SVP	3.15	3.39	4.11	4.47	4.58
pCT$^-$	TZVP	3.04	3.36	3.89	4.26	4.40
pCT$^-$	QZVP	3.00	3.35	3.84	4.19	4.33
pCT$^-$	aug-TZVP	2.98	3.33	3.37	3.55	3.57
pCT$^-$	extrapolated	2.94	3.32	<u>3.32</u>	<u>3.48</u>	<u>3.50</u>
pCT$^-$	oscillator strength	1.37	0.00	0.00	0.08	0.00

^{a} The molecular structures were optimized for the ground state at the MP2/TZVP level. Excitation energies for Rydberg and anionic states that demand diffuse basis functions in the basis set are underlined. The oscillator strengths calculated at the CC2/TZVP level are given.

CC2/QZVP level deviates by 0.45 eV from the CC2/aug-TZVP value. Diffuse anionic states, states in the continuum, as well as states with significant Rydberg character can be identified by augmenting the basis set with diffuse functions. They might lower the excitation energy even by more than 1 eV. The higher excited states (states 3–5) of the PYP chromophore models seem to require the use of diffuse basis functions. Diffuse states are not observed for the positively charged chromophores among the five lowest excited states. As previously shown, a second set of diffuse functions is sometimes necessary in order to approach the basis-set limit.[5] The excitation energies of the diffuse states are underlined in Tables 1–4. For pCA^{2-}, the first set of diffuse functions lowers the excitation energies by a factor of 2, implying that the electrons of the doubly charged anion are unbound. Thus, no reliable values for the excitation energies of pCA^{2-} can be obtained without stabilizing the system with counterions, solvent molecules, or by protein residues.

The present benchmark calculations show that the two lowest excited states of the investigated chromophores, which are also the biologically relevant states, are accurately described with TZVP basis sets. Moreover, the calculations show the importance of diffuse basis functions for higher excited states of anionic and neutral chromophores. The calculations also indicate the importance of assessing the basis set requirement individually for such chromophores.

Comparison of CC2 and B3LYP Excitation Energies. *General Trends.* The excitation energies and oscillator strengths, obtained at the B3LYP and CC2 levels, are compared in Figure 3 and Table 5. The excitation energies calculated for the cationic and neutral chromophore models at the B3LYP level are systematically smaller than the corresponding CC2 energies, with a deviation of −0.14 to +0.44 eV and a maximum deviation of 0.64 eV for some of the higher excited states (e.g., for pCA$^{-\prime\prime}$). At first glance, the B3LYP excitation energies seem to be in better agreement with experimental data than the CC2 ones, particularly for the smaller PYP chromophores. However, the oscillator strengths of the lower excited states of the anions obtained at the B3LYP level indicate that the TDDFT calculations suffer from problems, most likely related to the previously discussed DFT continuum problem.[5,55] The B3LYP calculations on some of the neutral chromophores also yield oscillator strengths that significantly differ from those obtained at the CC2 level, indicating that the states have different orbital character.

Cationic and Neutral Chromophores. The excitation energies of the PYP chromophore model pVP calculated at the B3LYP/aug-TZVP level are 0.15–0.44 eV smaller than the corresponding CC2 values. The B3LYP calculations yield very small oscillator strengths for the higher excited states, whereas four of the five states are bright at the CC2 level. The basis set convergence at the CC2 level shown in Figure 2 indicates that some of the higher excited states are not fully converged with the aug-TZVP basis set. When comparing the extrapolated values, a smaller difference between B3LYP and CC2 excitation energies of 0.02–0.32 eV is obtained.

For the pCA chromophore, which has an additional proto-nated carboxyl group relative to pVP, the first and the fifth

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dx.doi.org/10.1021/ct200215d |*J. Chem. Theory Comput.* 2011, 7, 2473–2484

Table 3. Basis-Set Dependence of the CC2 Excitation Energies (in eV) for the Five Lowest Excited Singlet States of the Green Fluorescent Protein Chromophore Models pHBDI, pHBDI$^-$, and pHBDI^{+a}

molecule	basis	1a	2a	3a	4a	5a
pHBDI$^+$	SVP	3.22	4.15	4.43	4.59	5.54
pHBDI$^+$	TZVP	3.15	4.03	4.36	4.44	5.32
pHBDI$^+$	QZVP	3.13	3.99	4.34	4.42	5.27
pHBDI$^+$	aug-TZVP	3.12	4.00	4.33	4.41	5.25
pHBDI$^+$	extrapolated	3.10	3.96	4.31	4.39	5.20
pHBDI$^+$	oscillator strength	1.09	0.02	0.00	0.00	0.10
pHBDI	SVP	3.88	4.01	4.70	4.71	5.55
pHBDI	TZVP	3.71	3.90	4.53	4.56	5.57
pHBDI	QZVP	3.68	3.89	4.50	4.52	5.45
pHBDI	aug-TZVP	3.66	3.87	4.49	4.51	5.01
pHBDI	extrapolated	3.63	3.86	4.46	4.47	<u>4.89</u>
pHBDI	oscillator strength	0.77	0.00	0.15	0.00	0.16
pHBDI$^-$	SVP	3.03	3.32	4.52	4.80	5.16
pHBDI$^-$	TZVP	2.92	3.30	4.30	4.54	4.57
pHBDI$^-$	QZVP	2.88	3.30	3.99	4.23	4.38
pHBDI$^-$	aug-TZVP	2.77	2.85	3.24	3.25	3.35
pHBDI$^-$	extrapolated	2.73	<u>2.85</u>	<u>2.93</u>	<u>2.94</u>	<u>3.16</u>
pHBDI$^-$	oscillator strength	1.17	0.00	0.07	0.00	0.00

[a] The molecular structures were optimized for the ground state at the MP2/TZVP level. Excitation energies for Rydberg and anionic states that demand diffuse basis functions in the basis set are underlined. The oscillator strengths calculated at the CC2/TZVP level are given.

Table 4. Basis-Set Dependence of the CC2 Excitation Energies (in eV) for the Five Lowest Excited Singlet States of the Retinal Protonated Schiff-Bases PSBT$^+$ and PSB11Me$_2^{+a}$

molecule	basis	1a	2a	3a	4a	5a
PSBT$^+$	SVP	2.23	3.45	4.34	4.72	4.89
PSBT$^+$	TZVP	2.17	3.35	4.22	4.54	4.73
PSBT$^+$	QZVP	2.15	3.33	4.19	4.52	4.70
PSBT$^+$	aug-TZVP^b	2.16	3.34	4.20	4.52	4.70
PSBT$^+$	extrapolated	2.14	3.32	4.17	4.50	4.67
PSBT$^+$	oscillator strength	1.92	0.50	0.10	0.01	0.05
PSB11Me$_2^+$	SVP	2.24	3.45	4.30	4.71	4.88
PSB11Me$_2^+$	TZVP	2.17	3.34	4.16	4.53	4.70
PSB11Me$_2^+$	QZVP	2.16	3.32	4.13	4.51	4.68
PSB11Me$_2^+$	aug-TZVP^b	2.16	3.32	4.14	4.51	4.68
PSB11Me$_2^+$	extrapolated	2.15	3.30	4.11	4.49	4.66
PSB11Me$_2^+$	oscillator strength	1.56	0.47	0.15	0.06	0.07

[a] The molecular structures were optimized for the ground state at the MP2/TZVP level. The oscillator strengths calculated at the CC2/TZVP level are given. [b] In the aug-TZVP calculations on retinals, the d and f functions were removed from the augmentation due to ground state convergence problems.

transitions are strong at the B3LYP level, while the CC2 calculations predict similarly as for the pVP model four strong transitions—among the five lowest excited states. The two lowest excitation energies obtained at the CC2 level are 0.30−0.35 eV larger than the experimental values, whereas the discrepancy at the B3LYP level is only 0.09−0.14 eV (cf. Comparison to Experiment section).

For the GFP and rhodopsin models (pHBDI$^+$, pHBDI, PSBT$^+$, and PSB11Me$_2^+$), the B3LYP and CC2 excitation energies and oscillator strengths are in qualitative agreement. The B3LYP excitation energies of pHBDI$^+$ and pHBDI are 0.2−0.3 eV smaller than the CC2 excitation energies, whereas the lowest excitation energies differ from the experimental values of the GFP and rhodopsin chromophores by 0.07−0.27 eV. The deviation from experiments at the CC2 level is 0.10−0.14 eV. The differences of 0.14 eV and −0.19 eV between the B3LYP and CC2 excitation energies of the first excited state of pHBDI$^+$ and pHBDI affect the conclusions drawn from the B3LYP and CC2 calculations. For the two lowest states of PSBT$^+$ and PSB11Me$_2^+$, the B3LYP and CC2 energies differ by 0.09−0.23 eV, whereas for the three higher excited states, the B3LYP energies are 0.37−0.63 eV smaller than the CC2 values.

Anionic Chromophores. The DFT ionization potential is given by the absolute orbital energy of the highest occupied molecular orbital (HOMO).[55] This implies that if the excitation energies exceed the DFT ionization potential (IP), the TDDFT calculations might yield unreliable results. In some cases, the excitation energies obtained using an increasing size of the basis set converge toward the HOMO energy corresponding to the first IP according to Koopmans' theorem.[5,55] This is especially problematic in the description of anions which have a weakly bound HOMO and

thus a very low IP. To avoid the DFT ionization problem, TDDFT calculations were performed with the anions stabilized by external point charges (pc-B3LYP), placed 5 Å from the molecular plane, both above and below the negatively charged substituent. The point charges lift the ionization threshold, ensuring that the lowest excited states are bound states at the DFT level. The dependence of the position and distribution of the point charges were not investigated, since the aim of the point charges is merely to avoid the DFT continuum problem.

The DFT IPs are much smaller than the Hartree−Fock self-consistent field (HF SCF) ones, because of the self-interaction problem, which causes problems for the anions as all excited states lie formally in the DFT continuum above the ionization threshold. The calculations show that the lowest excitation energies are only slightly dependent on the presence of the point charges, indicating that the states could be considered as some kind of metastable resonances in the DFT continuum. The high density of states of the anions becomes more sparse in the DFT calculation when point charges are used, showing the necessity of using point charges. Comparison of the B3LYP and CC2 oscillator strengths for the anionic chromophores shows that the B3LYP calculations often yield low-lying intruder states, which disappear when the anion is stabilized by point charges. This stabilization leads to an increase of the absolute HOMO energy, whereas the gap between the HOMO and the lowest-unoccupied molecular orbital (LUMO) remains nearly unaltered, indicating that excitation energies are less affected by the point charges than the IP. The excitation energies and oscillator strengths calculated with and without point charges are compared in Table 6 and Figure 4.

The external point charges red-shift the first excited state of pCA$^{-\prime}$ from 3.05 to 2.79 eV (Figure 4). The bright transition is blue-shifted by 0.08 eV from 3.34 to 3.42 eV, whereas the oscillator strengths remain nearly unchanged (not shown). The higher excitation energies are blue-shifted, yielding values in good agreement with the CC2 energies. The bright state at the CC2 level is the first excited state, whereas at the pc-B3LYP level, the second excited state has the largest oscillator strength.
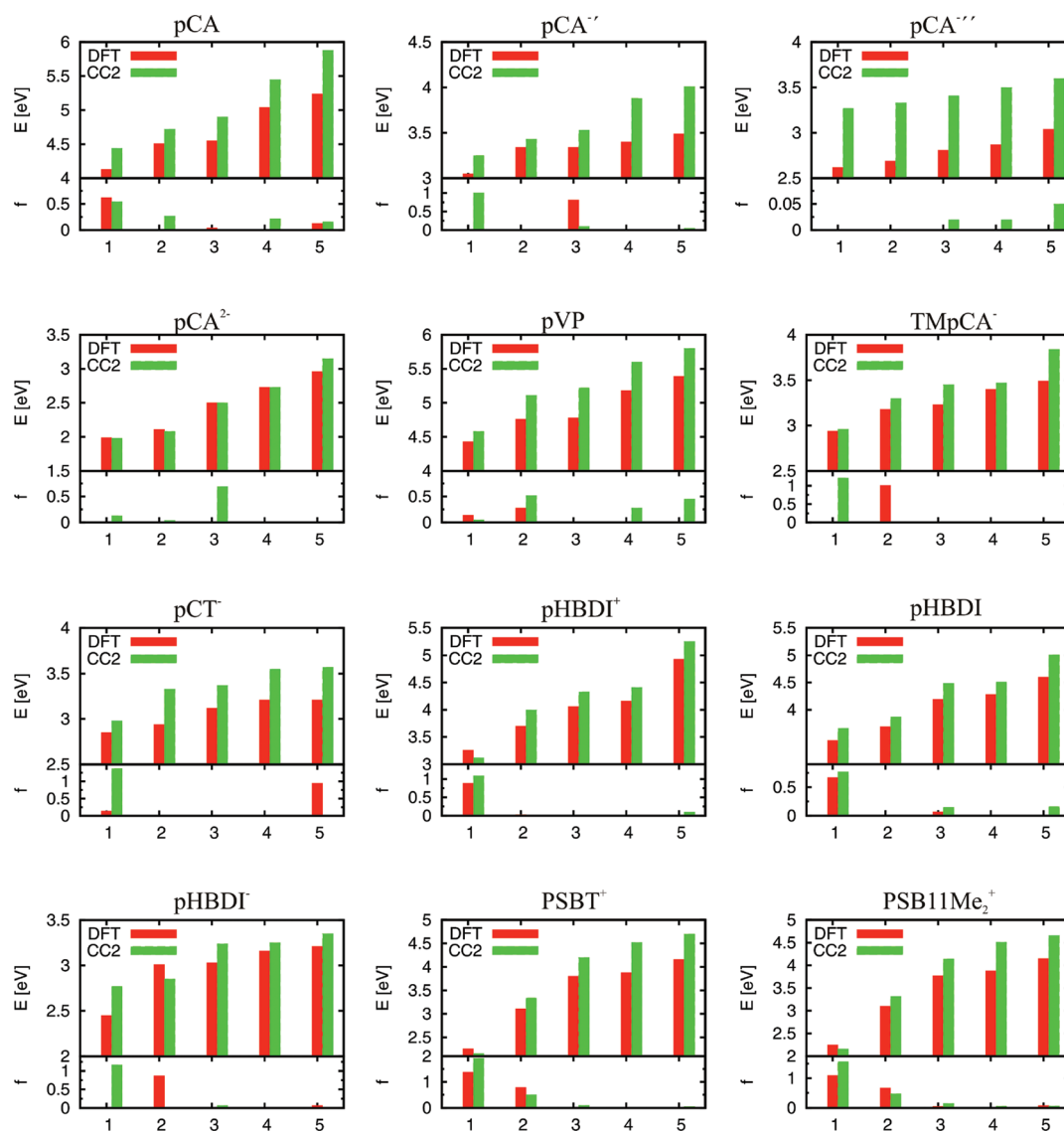
Figure 3. Comparison of the five lowest singlet excitation energies (in eV) and corresponding oscillator strengths calculated at the B3LYP and CC2 levels. All values are obtained using aug-TZVP basis sets. The integers on the x axis enumerate the excited states.

The excitation energies obtained for pCA$^{-\prime\prime}$ at the pc-B3LYP and CC2 levels are in qualitative agreement. The 10 lowest excited states of pCA$^{-\prime\prime}$ have a vanishing oscillator strength at the pc-B3LYP level. The external point charges increase the excitation energies of the chromophore in addition to producing a less dense spectrum. Still, at the pc-B3LYP level, the 10 lowest excitation energies are located in an energy interval of less than 1 eV, within 2.98 and 3.83 eV.

Similar results were obtained for the PYP chromophore models TMpCA$^-$ and pCT$^-$ and the GFP chromophore model pHBDI$^-$. Upon point-charge stabilization, the first excitation energy remains nearly unchanged, while the higher excitation energies are blue-shifted. For these anions, the first excited state has the largest oscillator strength at the CC2 level, whereas B3LYP and pc-B3LYP calculations suggest that the second and fifth excited states are the strongly light-absorbing ones.

The first CC2 excitation energy of the studied chromophores is smaller than the orbital energy of the HOMO orbital as obtained in the HF SCF calculations. The only exception is pCA^{2-}, having a

positive HOMO energy of 0.22 eV, whereas pCA$^{-\prime}$ and pHBDI$^-$ have only one state below the IP obtained at the HF SCF level. For TMpCA$^-$, three excited states lie below the ionization threshold of the HF SCF calculation. The rest of the studied chromophores have all five excited states below the HF SCF ionization threshold. The HOMO energies obtained in the HF SCF calculations are given in Table 5. The ionization potentials obtained at the CC2 level are not expected to deviate much from the HF SCF ones. For pCA$^{-\prime}$, the HOMO energy of 3.15 eV is 0.23 eV larger than the ionization threshold obtained at the coupled-cluster singles and doubles (CCSD) level.[56] The ionization and excitation thresholds of pCA$^{-\prime}$ (phenolate) and pCA$^{-\prime\prime}$ (carboxylate) have very recently been discussed by Zuev et al.[56]

pCA^{2-}. The doubly anionic PYP chromophore model pCA^{2-} was neutralized by four positive charges, placed 5 Å from the molecular plane above and below the two negatively charged substituents. At the pc-B3LYP level, the point charges shift the excitation energies by less than ±0.2 eV, and the oscillator strengths of the five lowest states are very small. At the pc-CC2

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dx.doi.org/10.1021/ct200215d |*J. Chem. Theory Comput.* 2011, 7, 2473–2484

Table 5. The Five Lowest Excitation Energies (E in eV) of the Biochromophore Models Calculated at the B3LYP/aug-TZVP Level[a]

molecule		1a	2a	3a	4a	5a	HOMO[b]
pCA	E	4.13	4.51	4.55	5.04	5.24	−6.29
pCA	f	0.62	0.00	0.04	0.00	0.13	(−8.40)
pCA$^{-\prime}$	E	3.05	3.34	3.34	3.40	3.49	−1.39
pCA$^{-\prime}$	f	0.00	0.00	0.81	0.00	0.00	(−3.15)
pCA$^{-\prime\prime}$	E	2.62	2.69	2.81	2.87	3.04	−1.49
pCA$^{-\prime\prime}$	f	0.00	0.00	0.00	0.00	0.00	(−4.66)
pCA^{2-}	E	1.99	2.11	2.50	2.73	2.96	+2.08
pCA^{2-}	f	0.00	0.00	0.00	0.00	0.00	(+0.22)
pVP	E	4.43	4.76	4.78	5.18	5.39	−5.86
pVP	f	0.14	0.28	0.00	0.01	0.00	(−7.92)
TMpCA$^-$	E	2.94	3.18	3.23	3.40	3.49	−1.50
TMpCA$^-$	f	0.00	1.01	0.00	0.00	0.00	(−3.23)
pCT$^-$	E	2.85	2.94	3.12	3.21	3.21	−1.71
pCT$^-$	f	0.14	0.00	0.01	0.01	0.95	(−3.39)
pHBDI$^+$	E	3.26	3.70	4.06	4.16	4.93	−9.05
pHBDI$^+$	f	0.89	0.03	0.00	0.02	0.01	(−10.9)
pHBDI	E	3.44	3.69	4.19	4.28	4.60	−5.62
pHBDI	f	0.67	0.00	0.07	0.01	0.00	(−7.55)
pHBDI$^-$	E	2.45	3.01	3.03	3.16	3.21	−1.30
pHBDI$^-$	f	0.00	0.87	0.00	0.00	0.07	(−2.89)
PSBT$^+$	E	2.26	3.11	3.80	3.88	4.16	−8.02
PSBT$^+$	f	1.38	0.78	0.01	0.00	0.03	(−9.75)
PSB11Me$_2^+$	E	2.25	3.10	3.77	3.88	4.15	−8.10
PSB11Me$_2^+$	f	1.10	0.67	0.05	0.01	0.08	(−9.87)

[a] The molecular structures were optimized for the ground state at the MP2/TZVP level. The oscillator strengths (f) and the highest occupied molecular orbital energies (HOMO) obtained in the B3LYP and HF SCF calculations are also reported. [b] The HOMO energies obtained at the HF SCF level are given within parentheses.

Table 6. Comparison of Excitation Energies (in eV) and Oscillator Strengths of the Anionic Chromophores Calculated at the B3LYP/aug-TZVP and pc-B3LYP/aug-TZVP Levels[a]

molecule	level and point charge			1a	2a	3a	4a	5a
pCA$^{-\prime}$	B3LYP	+1	E	2.79	3.42	3.58	3.66	3.75
pCA$^{-\prime}$	B3LYP	+1	f	0.00	0.77	0.00	0.00	0.00
pCA$^{-\prime}$	B3LYP		E	3.05	3.34	3.34	3.40	3.49
pCA$^{-\prime}$	B3LYP		f	0.00	0.00	0.81	0.00	0.00
pCA$^{-\prime\prime}$	B3LYP	+1	E	2.98	3.14	3.40	3.58	3.62
pCA$^{-\prime\prime}$	B3LYP	+1	f	0.00	0.00	0.00	0.01	0.00
pCA$^{-\prime\prime}$	B3LYP		E	2.62	2.69	2.81	2.87	3.04
pCA$^{-\prime\prime}$	B3LYP		f	0.00	0.00	0.00	0.00	0.00
pCA^{2-}	B3LYP	+2	E	1.81	2.31	2.68	2.76	2.83
pCA^{2-}	B3LYP	+2	f	0.00	0.00	0.00	0.00	0.00
pCA^{2-}	B3LYP		E	1.99	2.11	2.50	2.73	2.96
pCA^{2-}	B3LYP		f	0.00	0.00	0.00	0.00	0.00
pCA^{2-}	CC2	+2	E	1.86	2.59	2.83	2.91	3.27
pCA^{2-}	CC2	+2	f	0.00	0.00	0.00	0.01	0.00
pCA^{2-}	CC2		E	1.98	2.08	2.50	2.73	3.15
pCA^{2-}	CC2		f	0.13	0.04	0.69	0.00	0.00
TMpCA$^-$	B3LYP	+1	E	2.90	3.26	3.49	3.70	3.75
TMpCA$^-$	B3LYP	+1	f	0.00	0.99	0.00	0.00	0.00
TMpCA$^-$	B3LYP		E	2.94	3.18	3.23	3.40	3.49
TMpCA$^-$	B3LYP		f	0.00	1.01	0.00	0.00	0.00
pCT$^-$	B3LYP	+1	E	3.00	3.22	3.46	3.56	3.81
pCT$^-$	B3LYP	+1	f	0.00	1.04	0.00	0.00	0.00
pCT$^-$	B3LYP		E	2.85	2.94	3.12	3.21	3.21
pCT$^-$	B3LYP		f	0.14	0.00	0.01	0.01	0.95
pHBDI$^-$	B3LYP	+1	E	2.73	3.06	3.15	3.39	3.56
pHBDI$^-$	B3LYP	+1	f	0.00	0.93	0.00	0.00	0.00
pHBDI$^-$	B3LYP		E	2.45	3.01	3.03	3.16	3.21
pHBDI$^-$	B3LYP		f	0.00	0.87	0.00	0.00	0.07

[a] The CC2/aug-TZVP and pc-CC2/aug-TZVP values for pCA^{2-} are also reported.

level, the lowest excitation energy is red-shifted as compared to the CC2 value, while the higher excited states are blue-shifted. The three lowest lying states have nonvanishing oscillator strengths at the CC2 level, with the third state being the brightest one. The external point charges effectively damp the intensity of the five lowest excited states, at both levels of theory. The absorption spectra for pCA^{2-} calculated at the pc-B3LYP and pc-CC2 levels agree qualitatively despite a difference between some excitation energies by more than 0.4 eV

Comparison to MBGFT Calculations. The chromophores of PYP, GFP, and rhodopsin were recently studied with a MBGFT method by Ma and co-workers.[27] Uncontracted, universal, and almost even-tempered basis sets consisting of 40 primitive Gaussian basis functions of the s, p, and d types for the heavier atoms were employed in the calculations. An analogous basis set consisting of 30 basis functions was used for hydrogen. The basis-set convergence was assessed by adding basis functions in the π-electron region centered above and below bond centers.[27] Unfortunately, the accuracy and reliability of such nonstandard basis sets are not well established. The MBGFT method might treat molecular excited states more accurately than, e.g., TDDFT with today's functionals, which, however, cannot be assessed prior to a more systematic study.

Ma et al. reported MBGFT vacuum excitation energies for the chromophore models of PYP, GFP, and rhodopsin, with

deviations from experimental values of only 0.01−0.17 eV,[27] which is a much higher precision than obtained at any other computational level. However, some of the available experimental excitation energies are not obtained from gas-phase measurements but determined from measurements in solution or a protein environment. For example, the excitation energies of the GFP chromophore pHBDI measured in solvent (3.51 eV) and in protein (3.12 eV) differ significantly.[57,58] A recent calculation at the complete-active-space second-order perturbation theory (CASPT2) level using the newer zero-order Hamiltonian yields a lowest excitation energy of 3.58 eV,[19] which agrees well with the present CC2 value of 3.63 eV. This suggests that the experimental gas-phase value should be closer to 3.51 eV as obtained in solution than to 3.12 eV as measured in the protein. Thus, the excitation energy of 3.17 eV obtained in the MBGFT calculation is most likely 0.3−0.4 eV too small. Similar discrepancies might occur for the other chromophores, for which gas-phase measurements are not available, suggesting that the MBGFT approach might be less accurate than reported by Ma and co-workers.[27]

The B3LYP excitation energies are 0.10−0.33 eV higher than the corresponding MBGFT values, except for the anionic pHBDI$^-$ chromophore model, where B3LYP is 0.22 eV below

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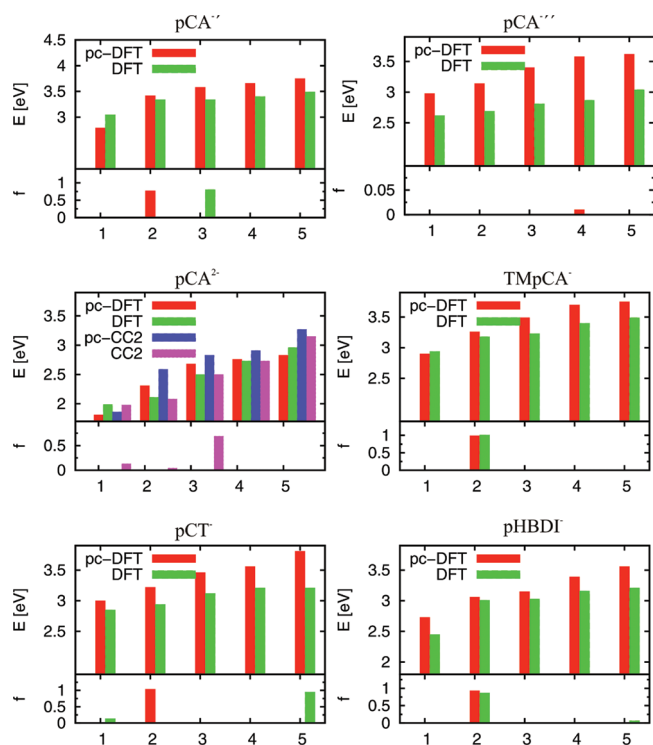dx.doi.org/10.1021/ct200215d | J. Chem. Theory Comput. 2011, 7, 2473−2484

Figure 4. Comparison of the excitation energies (in eV) and the corresponding oscillator strengths of the anionic chromophores calculated at the B3LYP level with those obtained with point-charge stabilization. The corresponding CC2 energies for pCA^{2-} are also shown. All values are obtained using aug-TZVP basis sets. The integers on the x axis enumerate the excited states.

the MBGFT value. However, as discussed above, the anionic chromophore suffers at the TDDFT level from the continuum problem. An external neutralizing point charge increases the TDDFT excitation energy to 2.73 eV, which is 0.06 eV larger than the excitation energy predicted by MBGFT. The pc-B3LYP excitation energies are 0.06−0.25 eV higher than the corresponding MBGFT energies, while the CC2 excitation energies are 0.06−0.45 eV larger than the corresponding MBGFT energies

Comparison to CASPT2 Calculations. *General Remarks.* Complete-active-space self-consistent-field (CASSCF) calculations combined with CASPT2 energy corrections have for a long time been the prime tool for studying ground and excited states of biochromophores. However, recent studies show that a number of older CASPT2 results are of limited value because the basis-set convergence has not been extensively assessed and the employed zeroth-order Hamiltonian was less accurate than originally anticipated. The recently introduced zeroth-order Hamiltonian in CASPT2 incorporates an empirical parameter and increases average excitation energies by 0.3 eV.[13,18,59] The CASPT2 excitation energies obtained using the new zeroth-order Hamiltonian seem to be in good agreement with experimental results provided that the employed basis sets are large enough. Valsson and Filippi[18] recently showed that the use of ground-state CASSCF optimized structures in CASPT2 studies results in artifacts when the excitation energies are sensitive to the geometry. The popular combination of CASSCF structures and single-point CASPT2 energies can thus lead to a qualitatively wrong character of the excited states, yielding results in complete disagreement with the consistent use of molecular structures and

excitation energies calculated at the CASPT2 level. Thus, many older CASSCF/CASPT2 studies of photochemical systems might have predicted incorrect reaction mechanisms.

Nevertheless, properly combined CASSCF and CASPT2 calculations are indispensable in studies of the excited state, when the reference state or the excited state has significant multiconfiguration character. Such situations occur quite frequently in photochemical processes, especially when the wave packets are approaching conical intersections. For vertical excitations, the lowest excited states of the investigated chromophores can be rather accurately expressed by expanding them in the configuration state basis of all singly and doubly excited determinants from a single-reference Slater determinant. At the *ab initio* level, the contributions from the double excitations are important as they take correlation effects into account, whereas in the TDDFT calculation the correlation effects are considered by the employed density functional. For many of the studied chromophores, CASPT2 calculations of the vertical excitation energies are not expected to yield more accurate excitation energies than obtained at the CC2 level. The computational costs for CASPT2 calculations increase rapidly with the size of the active space, hampering the feasibility of the CASPT2 calculations on larger molecules. For the GFP and rhodopsin chromophores, the approximations in the CASPT2 model and the inevitable limitations of the CASPT2 calculations introduce uncertainties of at least the same magnitude as the CC2 approximation, whereas for the PYP chromophore high-order correlation effects are more significant.

PYP Chromophores. A larger discrepancy between CASPT2 and CC2 excitation energies was obtained for the methyl ester of the pCA$^{-\prime}$ chromophore, recently studied at the CASPT2 level by Coto et al.[60] They obtained an excitation energy of 2.54 eV, which is 0.34 eV smaller than the experimental value of 2.88 eV.[25] The choice of the zeroth-order Hamiltonian is not mentioned in their work.[60] Experimentally, the absorption maximum of the methyl ester and the corresponding acid deviate in absorbance by only 3 nm, corresponding to an excitation energy shift of ±0.02 eV. Thus, the discrepancy between the CASPT2 and experimental results cannot be due to the methyl group. Recent CASPT2 calculations on pCA$^{-\prime}$ using the new standard IPEA shift of 0.25 eV as well as approximate third-order coupled-cluster (CC3) calculations yielded very similar excitation energies of 2.96 and 2.98 eV, respectively.[56] Depending on the choice of the zeroth-order Hamiltonian in the CASPT2 calculation, the excitation energies differ by about 0.3 eV. The present CC2 value of 3.19 eV calculated for the same chromophore model is 0.31 eV larger than the experimental value. The CC2 calculations overestimate the excitation energies for pCA$^{-\prime}$ and the other PYP chromophore models, whereas the older CASPT2 values for pCA$^{-\prime}$ are too small. The recent CASPT2 and CC3 excitation energies agree within 0.1 eV with experimental results.[25,56]

GFP Chromophores. The GFP chromophore illustrates another example where CASPT2 and CC2 excitation energies agree well. The present CC2 calculation yields an excitation energy of 3.63 eV for pHBDI, which is in almost perfect agreement with the CASPT2 value of 3.58 eV.[19] Gas-phase measurements of the excitation energies of pHBDI have not been reported, whereas the lowest excitation energy of pHBDI measured in solvents is 3.51 eV.[58] The corresponding excitation energy obtained for the chromophore in the protein is 3.12 eV,[57] indicating that the protein shift is much larger than the solvent shift.

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dx.doi.org/10.1021/ct200215d |*J. Chem. Theory Comput.* 2011, 7, 2473–2484

Table 7. Comparison of CC2, B3LYP, pc-B3LYP, and Experimental Excitation Energies (in eV) of the Bright State of the Anions[a]

molecule	CC2	B3LYP	pc-B3LYP	exp.	reference
pCA$^-$	3.19(1)	3.34(3)	3.42(2)	2.88	21
pCT$^-$	2.94(1)	2.85(1)^b	3.22(2)	2.70	20
TMpCA$^-$	2.91(1)	3.18(2)	3.26(2)		
pHBDI$^-$	2.73(1)	3.01(2)	3.06(2)	2.59, 2.76	70, 71

[a] The order of the excited state is given within parentheses. The calculated values are extrapolated CC2 values from Tables 1, 2, and 3. The B3LYP and pc-B3LYP data are gathered from Table 6. [b] The energy of the second bright state (the fifth state) at the B3LYP level is 3.21 eV.

Retinal Chromophores. The first excitation energy of isolated 11-*cis*-retinal at the CASPT2 level converged toward 2.28 eV prior to the gas-phase measurement.[61] After the experimental value was reported, CASPT2 and CC2 calculations yielded excitation energies of 2.05 and 2.10 eV, which are in fair agreement with the experimental value of 2.03 eV.[22,62,63] However, when the more recent zeroth-order Hamiltonian is employed, a CASPT2 excitation energy of 2.30 eV is obtained.[18] This zeroth-order Hamiltonian was designed to eliminate the mean error in CASPT2 excitation energies, and Valsson and Filippi conclude that the experimental value corresponding to the vertical transition is located around 2.34 eV.[18] The recent storage ring experiments do not render comparisons of experimental and computed retinal spectra easier.[26]

This illustrates that discrepancies between CASPT2 and CC2 excitation energies are not necessary due to the multireference character of the wave function and must be separately determined by a more careful analysis. In addition, gas-phase measurements of electronic excitation spectra of biochromophores are indispensable[22] and need to be interpreted with the help of simulated vibronic spectra. Unfortunately, in the case of retinals, such a simulation is currently not possible, as the excited state potential energy surface does not correspond to a harmonic potential.

Comparison to Experimental Results. *General Trends.* The B3LYP excitation energies seem to be in better agreement with experimental data than the CC2 ones, particularly for the smaller PYP chromophores. However, the oscillator strengths obtained at the B3LYP level indicate that the TDDFT calculations suffer from problems, most likely related to the previously discussed DFT continuum problem.[5,55] For pVP, pCA, pCA$^{-\prime}$, and pCT$^-$, the excitation energies obtained at the B3LYP level are indeed closer to the experimental values than the CC2 ones, whereas for pHBDI$^+$, pHBDI$^-$, PBST$^+$, and PBSMe$_2^+$, the CC2 excitation energies agree well with experimental results. For pCA$^{-\prime}$, TMpCA$^-$, and pHBDI$^-$, the first excited state is a spurious state at the B3LYP level. The excitation energies of the lowest bright states calculated at the CC2, B3LYP, and pc-B3LYP levels are compared to corresponding gas-phase values in Table 7. The comparison of the excitation energies for the first bright state of the anions shows that CC2 values are with deviations of −0.03 to +0.31 eV in much better agreement with experimental results than values obtained at the B3LYP (0.15−0.46 eV) and pc-B3LYP levels (0.30−0.52 eV). The range of the deviations is given in parentheses. For pCT$^-$, the

Table 8. The Extrapolated CC2 Excitation Energies As Well As the Excitation Energies Calculated at the B3LYP/aug-TZVP Level Compared to Experimental Data[a]

molecule	state	CC2	B3LYP	MBGFT	experiment	references
pVP	1	4.53	4.43	4.17	4.12	21
	2	4.76	4.76	4.60	4.75	21
pCA	1	4.39	4.13	3.94	4.04^b	68
	2	4.68	4.51	4.20	4.37^c	69
pCA$^{-\prime}$	1	3.19	3.05 (2.79)	2.95	2.88	25
pCA$^{-\prime\prime}$	1	3.28^d	2.62^d (2.98)	4.37^e	4.36^f	20
pCA^{2-}	1	1.89^g (1.86)	1.99 (1.81)	3.73^h	3.69^f	20
TMpCA$^-$	1	2.91	2.94 (2.90)	2.80	2.78^i	66
pCT$^-$	1	2.94	2.85 (3.00)	2.75	2.70	20
pHBDI$^+$	1	3.10	3.26	2.93	2.84,^{j} 2.99	24, 58
pHBDI$^-$	1	2.73	2.45 (2.73)	2.67	2.59, 2.76	70, 71
pHBDI	1	3.63	3.44	3.17	3.51^j	58
PSBT$^+$	1	2.14	2.26	2.03	2.00	22, 26
	2	3.32	3.11	3.10	3.22	22
PSB11Me$_2^+$	1	2.15	2.25	2.04	2.03	22
	2	3.30	3.10	3.01	3.18	22

[a] The pc-B3LYP/aug-TZVP and pc-CC2/aug-TZVP values are given in parentheses. The excitation energies obtained at the many-body Green's function theory (MBGFT) level by Ma et al.[27] are also reported. All experimental values that have not been recorded in the gas phase are printed in italics. [b] For the methyl ester, the experimental and CC2/aug-TZVP values are 4.06[21] and 4.46 eV. [c] Measured for the methyl ester, the CC2/aug-TZVP value is 4.73 eV. [d] The excitation energy of the lowest excited state. The fourth excitation energy is 3.45 eV (CC2), 2.87 eV (B3LYP), and 3.58 eV (pc-B3LYP). [e] The fourth excitation energy of the MBGFT calculation. [f] Measured in solvents. The value for pHBDI, measured in the protein, is 3.12 eV.[57] [g] The excitation energy of the second state is 2.00 eV (CC2), 2.11 eV (B3LYP), 2.59 eV (pc-CC2), and 2.31 eV (pc-B3LYP). [h] The second excitation energy of the MBGFT calculation. [i] Measured in the protein. [j] Vacuum value extrapolated from measurements in solution.

first and bright excited state at the B3LYP level is shifted up in energy when the molecule is stabilized by point charges. The first excited state of the anions is a dark state at the pc-B3LYP level, whereas at the CC2 level, the lowest excited state has large oscillator strengths.

PYP Chromophores. Theoretical prediction of spectra requires accurate determination of both excitation energies and intensities. However, the experimental spectrum is subject to vibrational broadening as well as intensity borrowing, which makes comparison of calculated and experimental spectra challenging.[23,64,65] The calculated excitation energies of all PYP chromophore models are compared to experimental data in Table 8.

In the case of pVP, the experimental spectrum is obtained using two-photon ionization spectroscopy, implying that the band intensities cannot be compared to the present calculations.[21] The strong dipole transitions obtained in the CC2 calculations appear at 5.04 and 5.5 eV, corresponding to a valence and a Rydberg transition, respectively. The two lowest experimental excitation energies are 4.12 and 4.75 eV. In the calculation, the two lowest transitions are weak and appear at 4.53 and 4.76 eV. The former is a valence band with a very small transition probability, whereas the latter state has significant Rydberg character, as suggested by the requirement of diffuse basis functions. At the B3LYP level, the lowest excitation energy of 4.43 eV is 0.3 eV larger than the experimental value, whereas the B3LYP and CC2 excitation energies of the second state are identical and in perfect agreement with experimental results.

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dx.doi.org/10.1021/ct200215d |*J. Chem. Theory Comput.* 2011, 7, 2473–2484

For pCA, the two lowest excitation energies have large oscillator strengths, making the comparison to experimental results easier. The excitation energy of the second state is measured only for the methyl ester. However, CC2 calculations show that pCA and its methyl ester have similar excitation energies. The CC2 excitation energies of pCA are 4.39 and 4.68 eV as compared to the experimental values of 4.04 and 4.37 eV. The B3LYP excitation energies of 4.13 and 4.51 eV also agree well with experimental values.

For pCA$^{-\prime}$, the CC2 excitation energy of 3.19 eV is 0.3 eV larger than the experimental value. The B3LYP calculation without point charges yields the bright excitation at 3.34 eV. However, this value is larger than the HOMO energy for pCA$^{-\prime}$, indicating that the B3LYP calculation might suffer from ionization problems. The pc-B3LYP calculation yields an excitation energy of 3.42 eV for the bright state, which is the second excited state in the calculation. For pCA$^{-\prime\prime}$ and pCA^{2-}, the pc-B3LYP and pc-CC2 calculations do not yield any bright states among the five lowest excited states. The calculated excitation energies for pCA^{2-} are 1−2 eV smaller than the experimental value of 3.69 eV, measured in the solvent.[20] The excitation energy of 3.67 eV obtained for pCA^{2-} at the CC2 level using the QZVP basis sets agrees well with the experimental result, suggesting that the solvent molecules mainly prevent the expansion of the electron density due to Coulomb repulsion. Thus, it seems to be possible to simulate the solvated dianion by omitting very diffuse basis functions in the CC2 calculation. The present study shows that CC2 generally overestimates the gas-phase values for the PYP chromophores by 0.24−0.39 eV.

The excitation energies for pCA$^{-\prime\prime}$, pCA^{2-}, and pHBDI cannot be directly compared to experimental values because they were obtained from measurements in solvents. The excitation energies for TMpCA^{-} and pHBDI were deduced from UV−vis spectra measured for the chromophores embedded in the protein. Comparison of the calculated excitation energies for TMpCA^{-} with the result from the measurement on the protein indicates that the protein shift is small. The CC2 and pc-B3LYP calculations yielded values of 2.91 and 2.90 eV as compared to the experimental value of 2.78 eV.[66] However, the first excited state at the B3LYP level has a very small oscillator strength. The first bright transition at the pc-B3LYP level occurs at 3.26 eV.

GFP Chromophores. Lammich et al. measured the electronic excitation spectra for pHBDI^{+} in the gas phase, since neutral molecules cannot be studied in storage ring experiments.[24] Their idea was that the cation might have very similar excitation energies as neutral pHBDI, because of the large distance between the positive charge and the light-absorbing part of the chromophore. The present calculations show that this assumption is wrong. The lowest excitation energies of pHBDI^{+} and pHBDI at the CC2 level differ by 0.53 eV, whereas the corresponding difference obtained at the B3LYP level is 0.18 eV. The good agreement between calculated and measured excitation energies for pHBDI^{+} suggests that the CC2 excitation energy obtained for pHBDI is also accurate, whereas the B3LYP value has a larger uncertainty. Furthermore, recent CASPT2 calculations on the pHBDI chromophore[19] yield an excitation energy in close agreement with the present CC2 value. Comparisons of the calculated excitation energy for pHBDI with those measured in the protein and in solution indicate that the solvent shift of the excitation energy is very small, whereas the protein shift is about 0.4 eV.

Retinal Chromophores. The two lowest excitation energies for the retinal models, PSBT^{+} and PSB11Me$_2$$^{+}$, have recently been measured in the gas phase.[22,26] The combined experimental and computational study suggests that the observed spectrum is a mixture of the ones for 6-*cis* and 6-*trans* retinal.[26] The present CC2 calculations on the 6-*cis* conformation yield values in very close agreement with the earlier experimental values,[22] indicating that the two lowest states are well described by low-order excitations from the ground state. The CC2 calculations also indicate that the recent interpretation of the measured spectrum should be carefully investigated. The photochemical properties of the protonated Schiff base retinals significantly differ from those of polyenes.[5,67]

The obtained CC2 excitation energies for the retinal models deviate less than 0.15 eV from experimental values. The two lowest excitation energies calculated at the B3LYP level agree within 0.08−0.26 eV with experimental values. The first excitation energy is slightly larger than that obtained experimentally, whereas the second excitation energy is smaller than the experimental value. Comparing gas-phase experiments to our extrapolated CC2/aug-QZVP results yields a good agreement for the rhodopsin and GFP chromophores with a maximum deviation of only 0.14 eV.

■ CONCLUSIONS

This work gives an overview on the performance of the CC2 and the B3LYP/TDDFT methods applied to excited states of chromophore model systems of the photoactive yellow protein (PYP), the green fluorescent protein (GFP), and rhodopsin. The CC2 method is a black box *ab initio* method that allows the assessment of basis set requirements for the five lowest singlet excited states of the chromophore models up to extrapolated aug-QZVP basis sets, thus yielding accurate benchmark data for comparison with experimental results.

The CC2 basis set requirements are fulfilled up to 0.15 eV at the triple-ζ level, except for the studied anions and for Rydberg states of the neutral chromophores. The excitation energies compare well to the experimental values, especially for the rhodopsin and GFP chromophore models. The excitation energies of the PYP chromophore models are not particularly well described at the CC2 level, with deviations up to 0.4 eV, when experimental gas-phase values are available.

B3LYP/TDDFT calculations show a similar performance with deviations of 0.2−0.3 eV from experimental results for the GFP and rhodopsin chromophore models. However, the anionic PYP chromophores are problematic at the B3LYP level, possibly due to the unphysically low ionization potential predicted at the DFT level. Stabilization of the anions with positive point charges seems to reduce this problem, while it still does not produce completely satisfactory results, when calculated intensities are taken into account.

The present work is the first compilation of accurately benchmarked excitation energies at the black box *ab initio* CC2 level, comprising the most important and experimentally most thoroughly investigated biochromophores. All molecules in our study are challenging for contemporary quantum chemical methods, and we provide an accurate benchmark with respect to all entering parameters. We hope that this work will serve as a reference point in the discussion of other computational methods where the assessment of parameter dependence is limited by computational costs.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sundholm@chem.helsinki.fi.

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dx.doi.org/10.1021/ct200215d |*J. Chem. Theory Comput.* 2011, 7, 2473−2484

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