

## Zn Coordination Chemistry: Development of Benchmark Suites for Geometries, Dipole Moments, and Bond Dissociation Energies and Their Use To Test and Validate Density Functionals and Molecular Orbital Theory

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**Abstract:** We present nonrelativistic and relativistic benchmark databases (obtained by coupled cluster calculations) of 10 Zn–ligand bond distances, 8 dipole moments, and 12 bond dissociation energies in Zn coordination compounds with O, S, NH<sub>3</sub>, H<sub>2</sub>O, OH, SCH<sub>3</sub>, and H ligands. These are used to test the predictions of 39 density functionals, Hartree–Fock theory, and seven more approximate molecular orbital theories. In the nonrelativistic case, the M05-2X, B97-2, and mPW1PW functionals emerge as the most accurate ones for this test data, with unitless balanced mean unsigned errors (BMUEs) of 0.33, 0.38, and 0.43, respectively. The best local functionals (i.e., functionals with no Hartree–Fock exchange) are M06-L and  $\tau$ -HCTH with BMUEs of 0.54 and 0.60, respectively. The popular B3LYP functional has a BMUE of 0.51, only slightly better than the value of 0.54 for the best local functional, which is less expensive. Hartree–Fock theory itself has a BMUE of 1.22. The M05-2X functional has a mean unsigned error of 0.008 Å for bond lengths, 0.19 D for dipole moments, and 4.30 kcal/mol for bond energies. The X3LYP functional has a smaller mean unsigned error (0.007 Å) for bond lengths but has mean unsigned errors of 0.43 D for dipole moments and 5.6 kcal/mol for bond energies. The M06-2X functional has a smaller mean unsigned error (3.3 kcal/mol) for bond energies but has mean unsigned errors of 0.017 Å for bond lengths and 0.37 D for dipole moments. The best of the semiempirical molecular orbital theories are PM3 and PM6, with BMUEs of 1.96 and 2.02, respectively. The ten most accurate functionals from the nonrelativistic benchmark analysis are then tested in relativistic calculations against new benchmarks obtained with coupled-cluster calculations and a relativistic effective core potential, resulting in M05-2X (BMUE = 0.895), PW6B95 (BMUE = 0.90), and B97-2 (BMUE = 0.93) as the top three functionals. We find significant relativistic effects ( $\sim 0.01$  Å in bond lengths,  $\sim 0.2$  D in dipole moments, and  $\sim 4$  kcal/mol in Zn–ligand bond energies) that cannot be neglected for accurate modeling, but the same density functionals that do well in all-electron nonrelativistic calculations do well with relativistic effective core potentials. Although most tests are carried out with augmented polarized triple- $\zeta$  basis sets, we also carried out some tests with an augmented polarized double- $\zeta$  basis set, and we found, on average, that with the smaller basis set DFT has no loss in accuracy for dipole moments and only  $\sim 10\%$  less accurate bond lengths.

### 1. Introduction

Zinc is an essential element for humans, primarily because it serves as a cofactor for a very large number of enzyme

reactions<sup>1,2</sup> (it is the second most abundant transition metal cation in biology<sup>3</sup>), and it is technologically important in ZnO photoluminescent materials and nanoparticles (quantum dots).<sup>4</sup> Zinc-binding proteins that perform essential functions in a variety of species, and for which accurate active-site modeling parameters are needed, include insulin, metallothionein, DNA topoisomerase, phosphotriesterase (an

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enzyme that hydrolyzes organophosphorus compounds like sarin<sup>5</sup>), zinc-finger proteins, matrix metalloproteinases (MMPs), the anthrax toxin lethal factor, alcohol dehydrogenase, human carbonic anhydrase,<sup>6</sup> cytidine deaminase,  $\beta$ -lactamases, and copper-zinc dismutase. In metalloproteins, Zn often functions as a Lewis acid, with catalysis occurring in its first coordination shell, or by electrostatically stabilizing reactants or intermediates in the active site. Zinc fluorescent sensors used to monitor labile Zn<sup>2+</sup><sup>7</sup> and chelating agents used in froth flotation<sup>8</sup> also operate by inner-shell coordination. Geometries, dipole moments, and bond dissociation energies of Zn coordination compounds are thus critical parameters for reliable simulations of biological function<sup>2,9–30</sup> and technological applications of Zn chemistry. Density functional theory (DFT) is a very promising electronic structure calculation tool for obtaining such parameters,<sup>31–33</sup> but systematic validation studies, which have not yet been reported, are required to understand the reliability of DFT calculations for Zn binding as well as the reliability of simpler semiempirical calculations that are often used because they are faster and less expensive.

The present paper presents nonrelativistic and relativistic validation suites of bond distances for 10 zinc–ligand complexes, dipole moments for 8 Zn model compounds, and bond dissociation energies (BDEs) for 12 zinc compounds. In obtaining all three parameter sets, we chose model compounds with Zn bonds to N, O, and S, which are the three most common first-coordination-shell atoms in zinc enzymes.<sup>25,34–37</sup> Although our first priority was to test model compounds representing biozinc centers, we also include one compound with Zn bonds to H, which occur at defect sites in ZnO crystals<sup>38</sup> and in hydrogen-doped zinc oxide thin films.<sup>39</sup> These data are then used to test practical electronic structure methods of both fundamental types: density functional theory (DFT)<sup>40</sup> and wave function theory (WFT).<sup>41,42</sup>

DFT methods evaluated with a nonrelativistic Hamiltonian include the five most accurate functionals<sup>43–54</sup> for metal–ligand bond energies in a recent study<sup>55</sup> of 21 metal–ligand complexes with 57 different density functionals and the two most accurate functionals<sup>48,51,55,56</sup> overall in that study (based on the 21 metal–ligand bond energies, 8 transition-metal dimer bond energies, 6 representative main-group atomization energies, 7 ionization potentials, 13 metal–ligand bond lengths, and 8 transition metal dimer bond lengths) plus five density functionals developed subsequently<sup>57–60</sup> and 26 other popular and representative density functionals<sup>43–46,48,49,51,54,56,61–78</sup> of various types. The NDO methods evaluated for comparison with DFT calculations are AM1,<sup>9,79–81</sup> MNDO,<sup>82,83</sup> MNDO/d,<sup>84,85</sup> PM3,<sup>86</sup> PM3(tm),<sup>86–90</sup> and the newer PM6 method.<sup>91</sup> (The PM3(tm) method is tested only for geometries and bond energies because it was not parametrized for dipole moments<sup>88</sup> and is specifically stated by its developers not to be used for that purpose.) The IEHT method that we test is self-consistent-charge density-functional tight-binding (SCC-DFTB).<sup>92–94</sup> For the nonrelativistic evaluations, we test the following: 39 density functionals, both local and nonlocal; ab initio Hartree–Fock (HF) theory; six semiempirical molecular orbital methods of the neglect of differential overlap (NDO) variety; and one

iterative extended Hückel theory (IEHT) method, which is also called a tight-binding method. These calculations involve testing nonrelativistic DFT calculations against nonrelativistic benchmarks. We then incorporate a relativistic effective core potential (ECP)<sup>95</sup> for Zn into the top ten methods resulting from this analysis and test these relativistic DFT calculations against new benchmarks that also incorporate relativistic effects via this ECP.

## 2. Data Sets and Computational Methods

**2.1. Basis Sets.** We use two basis sets in this work, and we will denote them B1 and B2. Basis set B1 is used for nonrelativistic DFT calculations. In this basis, Zn is represented by the 6-311+G(d,p) basis set of in *Gaussian 03*,<sup>96</sup> which is constructed from the earlier work of Wachters<sup>97</sup> and Hay<sup>98</sup> as modified by Raghavachari and Trucks,<sup>99</sup> who described both an “*spd*” basis and an “*spdf*” basis. The basis used here is the *spd* basis further polarized with a single *f* set with an exponent<sup>99</sup> of 1.62. The final Zn basis for B1 consists of a 15s11p6d1f primitive basis contracted to 10s7p4d1f, with the outer functions uncontracted. For H, C, N, O, and S in Series A, the basis set is MG3S', which denotes MG3S<sup>100</sup> with oxygen *f* functions removed to decrease computation time. Thus the MG3S' basis set is 6-311+G(2df,2p)<sup>100–102</sup> for H, C, and N, 6-311+G(2d)<sup>102–104</sup> for O, and the same as in G3Large<sup>105</sup> without core polarization functions for S.

Basis set B2 is used for relativistic DFT calculations, and for both nonrelativistic and relativistic WFT calculations (in particular, for CCSD(T) and CCSD benchmarks and for MP2 calculations used for extrapolation). We augment the Zn basis by adding two additional *f* functions specified by Raghavachari and Trucks,<sup>99</sup> with exponents of 0.486 and 5.40, and we restore the MG3S *f* functions to oxygen.

In both basis sets we use five spherical harmonic basis functions for *d* sets and seven spherical harmonic basis functions for *f* sets.

A smaller basis set will be discussed briefly in section 4.1.

**2.2. Core Orbitals and Relativistic Effects.** Relativistic effects may be divided into scalar relativistic effects and vector effects.<sup>106</sup> The most important vector relativistic effect is spin–orbit coupling, but, except for ZnH, all Zn-containing species treated in the present article are closed-shell singlets for which spin–orbit coupling vanishes. Spin–orbit coupling also vanishes for ZnH because it is a <sup>2</sup>S<sup>+</sup> state. Spin–orbit coupling is nonzero for O and S and was accounted for in all relativistic calculations (benchmarks and more approximate methods) by subtracting 0.02 kcal/mol (O) and 0.56 kcal/mol (S) from the calculated bond dissociation energies for processes that respectively produce O and S, based on atomic energy levels.<sup>107</sup>

Scalar relativistic effects are very important for 5d transition metals, important for 4d transition metals, and “small” but not negligible for 3d transition metals like Zn. For 3d and 4d transition metals, an adequate way to include scalar relativistic effects in either WFT or DFT is to replace the inner core orbitals by a relativistic effective core potential. (A recent study validating these procedures for PdCO may

be consulted for further discussion.<sup>108</sup>) In the present article, the inner core is defined as the next-to-largest noble gas core, which is sometimes called the “small core” prescription (thus the inner core for Zn has 10 electrons, whereas a large-core prescription (not used here) would treat 18 electrons as the core). In all WFT and DFT relativistic calculations, scalar relativistic effects at Zn are included by replacing the inner core electrons by the quasirelativistic multielectron-fit (MEFIT, *R*) pseudopotential of Preuss et al.<sup>95</sup> Note that we do *not* use the basis set developed<sup>95</sup> for use with this pseudopotential; all relativistic calculations in the present article use the B2 basis set.

In the present nonrelativistic calculations, all electrons are included explicitly with no effective core potential. In the nonrelativistic DFT calculations, all electrons are correlated. The nonrelativistic WFT calculations consist of an uncorrelated Hartree–Fock step followed by a correlated post-Hartree–Fock step. In the latter, the inner core (10 electrons) is not correlated. In extensive tests not presented here, we found that using the large-core prescription for the post-Hartree–Fock step gives significantly different geometries and should not be trusted.

**2.3. Benchmark Databases.** With the exception of ZnH<sub>2</sub>, for which the gas-phase equilibrium internuclear distance  $r_e$  has been obtained by high-resolution infrared emission spectroscopy,<sup>109,110</sup> experimental bond lengths and dipole moments have not yet been published for the model compounds in this study. Therefore our first goal is to assemble benchmark data sets. For this purpose, we first consider a set of ten Zn model compounds. For eight of these, in particular, ZnO, ZnS, Zn(NH<sub>3</sub>)<sub>2</sub><sup>2+</sup>, Zn(SCH<sub>3</sub>)<sup>+</sup>, Zn(H<sub>2</sub>O)<sub>2</sub><sup>2+</sup>, Zn(OH)<sub>2</sub>, ZnOH<sup>+</sup>, and ZnH<sub>2</sub>, coupled cluster theory<sup>111</sup> with single and double excitations<sup>112</sup> and quasiperturbative triple excitations (CCSD(T))<sup>113</sup> with basis B2 is applied to obtain the best estimates of accurate geometric parameters. The CCSD(T) method has been shown in multiple studies<sup>114–117</sup> to reliably and accurately reproduce experimental geometries for small transition-metal model compounds similar to those examined here when the basis set is large enough. For nonrelativistic benchmarks, the next-to-largest noble gas cores were frozen in these post-HF calculations; the relativistic best estimates use the quasirelativistic multielectron-fit (MEFIT,*R*) pseudopotential of Preuss et al. on Zn.<sup>95</sup> The Zn–ligand equilibrium bond-distance values obtained in these ways are shown in Table 1.

The two remaining model compounds, Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup>, in the geometry database were too large for CCSD(T)/B2 optimizations; therefore, our best estimates in these cases were obtained by extrapolation from MP2/B2 calculations. In particular, we noted that increasing the level of calculation from MP2/B2 to CCSD(T)/B2 for Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> uniformly increases the bond length, as shown in Table 2. It increases the Zn–N bond distance by 0.020 Å (nonrelativistic) and 0.022 Å (relativistic); we therefore increased the MP2/B2 calculated Zn–N  $r_e$  values by these amounts for Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> to obtain the best estimates in Table 1.

Best estimates of dipole moments were obtained by CCSD/B2 optimizations on an eight-compound data set: ZnO, ZnS,

**Table 1.** Best Estimates of Nonrelativistic and Relativistic Zn–Ligand Bond Distances Obtained by CCSD(T)/B2

compound	distance	$r_e$ (Å), nonrel	$r_e$ (Å), rel
ZnO	Zn–O	1.721	1.710
ZnS	Zn–S	2.077	2.067
Zn(NH <sub>3</sub> ) <sub>2</sub> <sup>2+</sup>	Zn–N	1.955	1.939
Zn(H <sub>2</sub> O) <sub>2</sub> <sup>2+</sup>	Zn–O	1.868	1.852
ZnOH <sup>+</sup>	Zn–O	1.764	1.757
Zn(SCH <sub>3</sub> ) <sup>+</sup>	Zn–S	2.181	2.170
Zn(OH) <sub>2</sub>	Zn–O	1.779	1.767
ZnH <sub>2</sub>	Zn–H	1.544	1.528 <sup>a</sup>
Zn(NH <sub>3</sub> ) <sub>3</sub> <sup>2+</sup>	Zn–N	2.016 <sup>b</sup>	2.005 <sup>b</sup>
Zn(NH <sub>3</sub> ) <sub>4</sub> <sup>2+</sup>	Zn–N	2.072 <sup>b</sup>	2.063 <sup>b</sup>

<sup>a</sup> For comparison, the experimental  $r_e$  value is 1.524 for ZnH<sub>2</sub>.<sup>110</sup>

<sup>b</sup> Estimated by extrapolation; cf. section 2.3.

**Table 2.** Comparison of Relativistic and Nonrelativistic MP2/B2 and CCSD(T)/B2 Bond Distances

compound	distance	$\Delta r_e$ (Å), nonrel <sup>a</sup>	$\Delta r_e$ (Å), rel <sup>a</sup>
ZnO	Zn–O	0.042	0.046
ZnS	Zn–S	0.028	0.030
Zn(NH <sub>3</sub> ) <sub>2</sub> <sup>2+</sup>	Zn–N	0.022	0.020
Zn(H <sub>2</sub> O) <sub>2</sub> <sup>2+</sup>	Zn–O	0.010	0.010
ZnOH <sup>+</sup>	Zn–O	0.015	0.017
Zn(SCH <sub>3</sub> ) <sup>+</sup>	Zn–S	0.040	0.040
Zn(OH) <sub>2</sub>	Zn–O	0.020	0.021
ZnH <sub>2</sub>	Zn–H	0.025	0.025

<sup>a</sup>  $\Delta r_e = [r_e(\text{CCSD(T)/B2}) - r_e(\text{MP2/B2})]$ .

**Table 3.** Nonrelativistic and Relativistic Best Estimates of Dipole Moments Calculated by the CCSD/B2 Method

compound	dipole moment (D) <sup>a</sup>	
	nonrelativistic	relativistic
ZnO	5.69	5.50
ZnS	5.73	5.47
Zn(NH <sub>3</sub> ) <sub>2</sub> <sup>2+</sup>	1.07	1.27
Zn(SCH <sub>3</sub> ) <sup>+</sup>	3.95	3.59
Zn(H <sub>2</sub> O) <sub>2</sub> <sup>2+</sup>	0.27	0.39
ZnOH <sup>+</sup>	4.51	4.27
Zn(NH <sub>3</sub> ) <sub>2</sub> (OH) <sub>2</sub>	3.86	3.80
Zn(NH <sub>3</sub> )(OH) <sup>+</sup>	7.40	7.34

<sup>a</sup> 1 D  $\equiv$  1 Debye. For ions, the origin is at the center of mass of the nuclei.

Zn(NH<sub>3</sub>)<sub>2</sub><sup>2+</sup>, Zn(SCH<sub>3</sub>)<sup>+</sup>, Zn(H<sub>2</sub>O)<sub>2</sub><sup>2+</sup>, ZnOH<sup>+</sup>, Zn(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub>, and Zn(NH<sub>3</sub>)(OH)<sup>+</sup> (Table 3). Benchmarks for Zn–ligand bond dissociation energies were obtained for a 12-compound data set: ZnO, ZnS, Zn(NH<sub>3</sub>)<sub>2</sub><sup>2+</sup>, Zn(OH)<sub>2</sub>, ZnH<sub>2</sub>, Zn(SCH<sub>3</sub>)<sup>+</sup>, Zn(H<sub>2</sub>O)<sub>2</sub><sup>2+</sup>, ZnOH<sup>+</sup>, Zn(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub>, Zn(NH<sub>3</sub>)(OH)<sup>+</sup>, Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup>, and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> (Table 4). For molecules that include ammonia groups in addition to other ligands, the Zn–N BDE is the one considered, as shown in the last two rows of Table 4. Bond dissociation energies for four of these molecules, Zn(NH<sub>3</sub>)(OH)<sup>+</sup>, Zn(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub>, Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup>, and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup>, were again extrapolated from MP2/B2 calculations as they proved too large for CCSD(T) optimizations. Energies for Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> were estimated based on the 1.29 kcal/mol (nonrelativistic) and 1.42 kcal/mol (relativistic) decrease in BDE for Zn(NH<sub>3</sub>)<sub>2</sub><sup>2+</sup> from the MP2 to the CCSD(T) level (Table 5). The mean decrease in

**Table 4.** Best Estimates of Nonrelativistic and Relativistic Zn–Ligand Bond Dissociation Energies (BDEs in kcal/mol) Obtained by CCSD(T)/B2

compound	dissociation products	BDE (kcal/mol), nonrel	BDE (kcal/mol), rel
ZnO	Zn, O	83.51	80.30
ZnS	Zn, S	61.92	58.00
Zn(NH <sub>3</sub> ) <sup>2+</sup>	Zn <sup>2+</sup> , NH <sub>3</sub>	129.00	134.15
Zn(H <sub>2</sub> O) <sup>2+</sup>	Zn <sup>2+</sup> , H <sub>2</sub> O	96.83	99.78
ZnOH <sup>+</sup>	Zn <sup>2+</sup> , OH <sup>−</sup>	428.18	435.66
Zn(SCH <sub>3</sub> ) <sup>+</sup>	Zn <sup>2+</sup> , SCH <sub>3</sub> <sup>−</sup>	420.60	433.84
Zn(OH) <sub>2</sub>	ZnOH <sup>+</sup> , OH <sup>−</sup>	256.81	258.71
ZnH <sub>2</sub>	ZnH, H	78.72	78.90
Zn(NH <sub>3</sub> ) <sub>3</sub> <sup>2+</sup>	Zn(NH <sub>3</sub> ) <sub>2</sub> <sup>2+</sup> , NH <sub>3</sub>	61.74 <sup>a</sup>	60.67 <sup>a</sup>
Zn(NH <sub>3</sub> ) <sub>4</sub> <sup>2+</sup>	Zn(NH <sub>3</sub> ) <sub>3</sub> <sup>2+</sup> , NH <sub>3</sub>	46.81 <sup>a</sup>	46.04 <sup>a</sup>
Zn(NH <sub>3</sub> ) <sub>2</sub> (OH) <sub>2</sub>	Zn(NH <sub>3</sub> )(OH) <sub>2</sub> , NH <sub>3</sub>	10.31 <sup>a</sup>	8.87 <sup>a</sup>
Zn(NH <sub>3</sub> )(OH) <sup>+</sup>	ZnOH <sup>+</sup> , NH <sub>3</sub>	79.31 <sup>a</sup>	81.14 <sup>a</sup>

<sup>a</sup> Estimated by extrapolation; cf. section 2.3.**Table 5.** Comparison of Relativistic and Nonrelativistic MP2/B2 and CCSD(T)/B2 Bond Dissociation Energies (BDEs)

compound	dissociation products	$\Delta_{\text{BDE}}$ (kcal/mol), nonrel <sup>a</sup>	$\Delta_{\text{BDE}}$ (kcal/mol), rel <sup>a</sup>
ZnO	Zn, O	−31.75	−31.30
ZnS	Zn, S	−16.82	−17.17
Zn(NH <sub>3</sub> ) <sub>2</sub> <sup>2+</sup>	Zn <sup>2+</sup> , NH <sub>3</sub>	−1.29	−1.42
Zn(H <sub>2</sub> O) <sub>2</sub> <sup>2+</sup>	Zn <sup>2+</sup> , H <sub>2</sub> O	−0.94	−1.02
ZnOH <sup>+</sup>	Zn <sup>2+</sup> , OH <sup>−</sup>	0.34	0.19
Zn(SCH <sub>3</sub> ) <sup>+</sup>	Zn <sup>2+</sup> , SCH <sub>3</sub> <sup>−</sup>	−1.63	1.73
Zn(OH) <sub>2</sub>	ZnOH <sup>+</sup> , OH <sup>−</sup>	−2.41	−2.79
ZnH <sub>2</sub>	ZnH, H	1.02	0.77

<sup>a</sup>  $\Delta_{\text{BDE}} = [\text{BDE (CCSD(T)/B2)} - \text{BDE (MP2/B2)}]$ .

BDEs for Zn(NH<sub>3</sub>)<sub>2</sub><sup>2+</sup>, Zn(OH)<sub>2</sub>, Zn(H<sub>2</sub>O)<sub>2</sub><sup>2+</sup>, and ZnOH<sup>+</sup> from MP2/B2 to CCSD(T)/B2 was 1.24 kcal/mol (nonrelativistic) and 1.36 kcal/mol (relativistic); we therefore estimate CCSD(T) BDEs for Zn(NH<sub>3</sub>)(OH)<sup>+</sup> and Zn(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub> based on these values. BDEs for the remaining eight molecules were obtained from CCSD(T)/B2 optimizations.

**2.4. Density Functionals.** The properties of the density functionals we tested are given in Table 6. The five most accurate functionals in ref 55 for metal–ligand bond energies were TPSS1KCIS,<sup>43–47</sup> O3LYP,<sup>48–50</sup> MPW1KCIS,<sup>43–45,51,52</sup> TPSSh,<sup>53</sup> and B97-2.<sup>54</sup> The two most accurate functionals (overall) in ref 55 were G96LYP<sup>48,56</sup> and MPWLYP1M,<sup>48,51,55</sup> BLYP<sup>48,64</sup> and MOHLYP<sup>48,49,55</sup> were also among the five best functionals overall and are also tested here. The new functionals we test are as follows: M05,<sup>57</sup> M05-2X,<sup>58</sup> M06-L,<sup>59</sup> M06,<sup>60</sup> M06-2X,<sup>61</sup> and G96LYP1M.<sup>118</sup> In addition to these, we tested an assortment of popular functionals with varying performance ranges.<sup>43–46,48,49,51,55,56,61–78</sup>

The functional set tested here comprises 1 local spin density approximation (LSDA), 5 generalized-gradient approximation (GGA), 7 generalized-gradient exchange (GGE), 3 GGE with scaled correlation (GGSC), 10 hybrid GGA (HGGA), 9 hybrid meta GGA (HMGGA), and 4 meta GGA (MGGA) methods (see Table 6). LSDA functionals depend on the spin densities; GGA functionals depend on the gradient of the spin densities as well as the spin densities themselves; HGGA functionals depend on the percentage of

**Table 6.** Summary of the DFT Methods Evaluated in This Study<sup>a</sup>

functional	type	X	$\tau$ in E or C?	refs
B1LYP	HGGA	25	neither	48,64,71
B3LYP	HGGA	20	neither	48,67,68
B97-2	HGGA	21	neither	54
BLYP	GGA	0	neither	48,64
BP86	GGA	0	neither	63,64
BVWN5	GGE	0	neither	62,64
G96HLYP	GGSC	0	neither	48,55,56
G96LYP	GGA	0	neither	48,56
G96LYP1M <sup>b</sup>	GGSC	0	neither	118
G96VWN5	GGE	0	neither	56,62
$\tau$ -HCTH	MGGA	0	exchange	73,75
M05	HMGGA	28	both	57
M05-2X	HMGGA	56	both	58
M06	HMGGA	27	both	60
M06-2X	HMGGA	54	both	60
M06-L	MGGA	0	both	59
MOHLYP	GGSC	0	neither	48,49,55
MPW1B95	HMGGA	31	correlation	51,69,77
MPW1KCIS	HMGGA	15	correlation	43–45,51,52
mPW1PW <sup>c</sup>	HGGA	25	neither	51,65
mPWLYP	GGA	0	neither	48,51
MPWLYP1M	HGGA	5	neither	48,51,55
mPWVWN5	GGE	0	neither	51,62
O3LYP	HGGA	11.61	neither	48–50
OLYP	GGA	0	neither	48,49
OPWL	GGE	0	neither	49,66
OV5LYP	HGGA	0	neither	48,49,62
OVWN5	GGE	0	neither	49,62
PBEh <sup>d</sup>	HGGA	25	neither	70,74
PBELYP	HGGA	0	neither	48,70
PBEVWN5	GGE	0	neither	62,70
PW6B95	HMGGA	28	correlation	78
SVWN5	LSDA	0	neither	61,62
TPSS	MGGA	0	both	46
TPSS1KCIS	HMGGA	13	both	43–47
TPSSh	HMGGA	10	both	53
TPSSVWN5	GGE	0	exchange	46,62
VSXC <sup>e</sup>	MGGA	0	both	72
X3LYP	HGGA	21.8	neither	38,44,45,68

<sup>a</sup> GGA: generalized-gradient approximation; GGE: generalized-gradient exchange; GGSC: generalized-gradient exchange with scaled correlation; HGGA: hybrid GGA; HMGGA: hybrid meta GGA; LSDA: local spin density approximation; MGGA: meta GGA; X = percentage of Hartree–Fock exchange; E = exchange; C = correlation. <sup>b</sup> G96LYP1M is like G98HLYP except that the gradient correction to the correlation energy is multiplied by 0.54 instead of 0.50. <sup>c</sup> Same as mPWO, mPW1PW91, and MPW25. <sup>d</sup> Same as PBE0 and PBE1PBE. <sup>e</sup> Same as VS98.

Hartree–Fock (HF) exchange, the density gradients, and the spin densities; MGGA functionals depend on the spin kinetic energy densities  $\tau_{\sigma}$ , the spin density gradients, and the spin densities; and HMGGA functionals depend on  $\tau_{\sigma}$ , HF exchange, the density gradients, and the spin densities. GGE methods combine GGA exchange with LSDA correlation, and in GGSC, a relatively new approach,<sup>55</sup> the Kohn–Sham operator is defined by

$$F = F^{\text{SE}} + F^{\text{GCE}} + F^{\text{LC}} + (Y/100)F^{\text{GCC}} \quad (1)$$

where  $F^{\text{SE}}$  is the Slater local exchange functional,<sup>55</sup>  $F^{\text{GCE}}$  is the gradient correction to the LSDA exchange,  $F^{\text{LC}}$  is the LSDA correlation functional, and  $F^{\text{GCC}}$  is the gradient correction to the LSDA correlation, and  $Y$  is the percentage



of the gradient correction to correlation that is included. Here we set  $Y = 50$  in two of the GGSC functionals in this study, G96HLYP and MOHLYP, as was done in previous work,<sup>55</sup> and we set  $Y = 54$  in another.<sup>118</sup> For each theory level we specify the percentage  $X$  of Hartree–Fock exchange, and whether  $\tau_\sigma$  is included in the exchange and/or correlation functionals.

**2.5. Computational Details.** CCSD, CCSD(T), DFT, AM1, PM3, and MNDO calculations were carried out using *Gaussian 03* or a locally modified version of *Gaussian 03*<sup>95</sup> on the Minnesota Supercomputing Institute core resources and on an Alienware MJ-12 dual-CPU workstation running under the SUSE Linux Professional 9.3 operating system. MNDO/d and PM3(tm) calculations were obtained on the Alienware MJ-12 with the SPARTAN '02 and '04 Linux software packages.<sup>119</sup> PM6 calculations were performed using MOPAC 2007<sup>120</sup> on Alienware Area-51m and Alienware Sentia machines running Windows XP. SCC-DFTB calculations were done using DFTB/DYLAX<sup>92–94</sup> on the Minnesota Supercomputing Institute core resources.

### 3. Results

All nonrelativistic DFT methods and HF theory were tested using the B1 basis set against nonrelativistic B2 benchmark values; the top ten functionals resulting from this analysis were then evaluated using the aforementioned pseudopotential<sup>95</sup> against relativistic B2 benchmark values.

**3.1. Nonrelativistic Calculations.** We first compare the nonrelativistic geometric parameters, dipole moments, and bond dissociation energies obtained by the 39 chosen DFT functionals, HF theory, the six NDO methods, and SCC-DFTB to the nonrelativistic benchmark values we reported in section 2. We included DFT levels with a fairly wide variation in Hartree–Fock exchange, from 0 to 56% as well as HF theory with 100% Hartree–Fock exchange. The quality of our results was evaluated by mean unsigned errors (MUEs) representing the average absolute deviations from calculated benchmark values and also by mean signed errors (MSEs) used to detect systematic error. The mean unsigned errors for DFT and Hartree–Fock Zn–ligand equilibrium bond distances are reported in Table 7, and Table 8 gives analogous results for semiempirical molecular orbital theory. Tables 9 and 10 give the mean unsigned errors for model-compound dipole moments, and Tables 11 and 12 list MUEs for bond dissociation energies. Corresponding MSEs are provided in the Supporting Information.

The balanced mean unsigned error (BMUE) is a unitless quantity that normalizes MUEs for each parameter against the average error over all methods for that parameter and thus serves as a valuable criterion to evaluate the overall performance of each technique

$$\text{BMUE} = \{[\text{MUE}(\text{in } \text{\AA})/\text{AMUE}(\text{in } \text{\AA})] + [\text{MUE}(\text{in D})/\text{AMUE}(\text{in D})] + [\text{MUE}(\text{in kcal/mol})/\text{AMUE}(\text{in kcal/mol})]\}/3 \quad (2)$$

where AMUE is the average mean unsigned error, i.e., the mean of all MUEs for bond distances (in  $\text{\AA}$ ), dipole moments (in D), or bond dissociation energies (in kcal/mol). Table 13 gives nonrelativistic BMUEs for all methods except PM3-

**Table 7.** Mean Unsigned Errors (MUEs) in DFT and HF Zn–Ligand Bond Distance for Ten Zinc–Ligand Complexes (Nonrelativistic)<sup>a</sup>

functional	MUE ( $\text{\AA}$ )	functional	MUE ( $\text{\AA}$ )
X3LYP	0.0069	M06-2X	0.0169
PW6B95	0.0072	MPWLYP1M	0.0175
M05-2X	0.0078	G96LYP	0.0177
B3LYP	0.0080	mPWLYP	0.0205
MPW1KCIS	0.0080	OLYP	0.0215
B1LYP	0.0084	BLYP	0.0223
mPW1PW	0.0089	HF	0.0224
PBEh	0.0089	G96LYP1M	0.0236
PB86	0.0090	G96HLYP	0.0241
B97-2	0.0090	OV5LYP	0.0244
TPSSH	0.0094	PBELYP	0.0291
TPSS1KCIS	0.0097	TPSSVWN5	0.0309
MPW1B95	0.0105	G96VWN5	0.0318
M06-L	0.0109	OVWN5	0.0355
TPSS	0.0113	OPWL	0.0358
$\tau$ -HCTH	0.0133	mPWVWN5	0.0359
O3LYP	0.0139	PBEVWN5	0.0368
M05	0.0147	BVWNS	0.0377
M06	0.0147	SVWN5	0.0410
VSXC	0.0151	MOHLYP	0.0769

<sup>a</sup> Nonrelativistic DFT/B1 tested against nonrelativistic CCSD(T)/B2.

**Table 8.** Mean Unsigned Errors (MUEs) in NDO and SCC-DFTB Zn–Ligand Bond Distance for Ten Zinc–Ligand Complexes (Nonrelativistic)

method	MUE ( $\text{\AA}$ )
SCC-DFTB	0.043
PM3(tm)	0.061
AM1	0.063
PM3	0.069
PM6	0.077
MNDO(d)	0.078
MNDO	0.082

(tm), which is unsuitable<sup>88</sup> for transition-metal dipole moment calculations and which returned very large errors in dipole moments for our compound set; and SCC-DFTB, which gave enormously inaccurate bond dissociation energies. For these reasons PM3 (tm) and SCC-DFTB were not included in calculating AMUEs.

Table 14 shows results for a smaller basis set discussed in section 4.1

**3.2. Relativistic Calculations.** We used the same error measures for the relativistic comparisons. Table 15 lists relativistic BMUEs for the top ten functionals from Table 13, and tables analogous to Tables 7, 9, and 11, but for relativistic calculations, are given in the Supporting Information.

## 4. Discussion

**4.1. Nonrelativistic Tests.** The X3LYP functional shows the best performance for bond lengths in the nonrelativistic calculations, followed by PW6B95, M05-2X, and B3LYP. These methods all have  $20 \leq X \leq 56$ . The next two functionals in the ranking have  $X = 15$  and  $X = 25$ . The

**Table 9.** Mean Unsigned Errors (MUEs) in DFT and HF Dipole Moment for Eight Zinc–Ligand Complexes (Nonrelativistic)<sup>a</sup>

functional	MUE (D)	functional	MUE (D)
M05-2X	0.19	OV5LYP	0.47
B97-2	0.26	OLYP	0.51
M05	0.27	TPSS	0.54
mPW1PW	0.28	TPSSVWN5	0.57
MPW1B95	0.29	MPW1KCIS	0.61
PBEh	0.29	VSXC	0.63
PW6B95	0.33	G96VWN5	0.63
O3LYP	0.36	G96HLYP	0.70
M06-2X	0.37	G96LYP1M	0.70
TPSSh	0.38	mPWVWN5	0.72
TPSS1KCIS	0.39	BP86	0.73
B1LYP	0.39	MPWLYP1M	0.75
OVWN5	0.39	PBEVWN5	0.75
OPWL	0.39	PBELYP	0.81
MOHLYP	0.40	BVWN5	0.82
$\tau$ -HCTH	0.41	BLYP	0.85
X3LYP	0.43	mPWLYP	0.85
M06-L	0.43	HF	0.87
B3LYP	0.44	SVWN5	0.89
M06	0.45	G96LYP	0.90

<sup>a</sup> Nonrelativistic DFT/B1 tested against nonrelativistic CCSD/B2.**Table 10.** Mean Unsigned Errors (MUEs) in NDO and SCC-DFTB Dipole Moment for Eight Zinc–Ligand Complexes

method	MUE (D)
AM1	0.79
PM3	0.86
PM6	1.15
MNDO	1.28
MNDO(d)	1.29
SCC-DFTB	1.45

first 25 functionals have MUE < 0.022 Å, whereas Table 8 shows that even the best of the semiempirical molecular orbital methods has MUE = 0.043 Å.

It is interesting to compare the results in Table 7 to a previous study<sup>121</sup> of bond lengths in van der Waals complexes that included results for Zn<sub>2</sub>, ZnNe, ZnAr, and ZnKr by 19 different density functionals. If one computes the mean unsigned errors on those four compounds, the best result (0.28 Å) was obtained by using M05-2X. (The mean unsigned error is larger than the typical value in the present work because the van der Waals complexes have flatter potentials than those for the covalent and coordinate covalent bonds studied here.) Seven other functionals included in that study are also included here, and their mean unsigned errors for the four Zn-containing van der Waals molecules are (in Å) as follows: PW6B95, 0.38; PBEh, 0.41; MPW1B95, 0.44; M05, 0.45; TPSSh, 0.59; TPSS, 0.59; and mPW1PW, 0.67. It is encouraging that the M05-2X and PW6B95 density functionals perform relatively well in both the previous and the present studies.

Table 9 shows that the M05-2X functional predicts the most accurate nonrelativistic dipole moments by a large margin. The B97-2, M05, mPW1PW, MPW1B95, and PBEh

**Table 11.** Mean Unsigned Errors (MUEs) in DFT and HF Bond Dissociation Energy (BDE) for Twelve Zinc–Ligand Complexes (Nonrelativistic)<sup>a</sup>

functional	MUE (kcal/mol)	functional	MUE (kcal/mol)
M06-2X	3.30	G96HLYP	7.27
M05	3.34	TPSSh	7.28
M06	3.80	G96LYP1M	7.33
B97-2	3.94	OV5LYP	7.47
B1LYP	4.26	mPWVWN5	7.50
M05-2X	4.30	OLYP	7.74
MPW1B95	5.16	OVWN5	7.87
mPW1PW	5.24	OPWL	7.88
PW6B95	5.26	PBEVWN5	7.90
M06-L	5.40	VSXC	8.04
B3LYP	5.41	TPSS	8.41
O3LYP	5.51	MPWLYP1M	8.49
X3LYP	5.64	BLYP	8.67
TPSSVWN5	5.97	PBELYP	8.89
PBEh	5.99	BP86	9.06
TPSS1KCIS	6.51	mPWLYP	9.49
MPW1KCIS	6.59	G96LYP	9.50
G96VWNS	6.66	MOHLYP	13.04
$\tau$ -HCTH	6.73	HF	15.02
BVWN5	6.99	SVWN5	22.06

<sup>a</sup> Nonrelativistic DFT/B1 tested against nonrelativistic CCSD(T)/B2.**Table 12.** Mean Unsigned Errors (MUEs) in NDO and SCC-DFTB Bond Dissociation Energy (BDE) for Twelve Zinc–Ligand Complexes

method	MUE (kcal/mol)
PM6	13.72
PM3	20.43
AM1	27.37
MNDO(d)	28.19
MNDO	31.26
PM3(tm)	84.96
SCC-DFTB	302.13

functionals are in second through sixth place, with MUE ≤ 0.29 D. In contrast the top semiempirical molecular orbital method, AM1, has MUE = 0.79 D (Table 10). We note that SCC-DFTB is more expensive than NDO methods, but—despite its name—its performance is more similar to other NDO methods than to DFT.

The M06-2X functional is the top DFT method for nonrelativistic bond dissociation energies (Table 11), followed closely by the M05, M06, B97-2, B1LYP, and M05-2X functionals. Once again the NDO methods prove inferior, with PM6 as the best method in this class with MUE = 13.72 kcal/mol. Most notably, SCC-DFTB rendered highly inaccurate BDEs for our compound set, with MUE = 302.13 kcal/mol. In the remainder of the discussion we focus on the unitless balanced MUE (BMUE), which takes account of all three parameters examined here: bond distances, dipole moments, and bond dissociation energies.

Overall, for nonrelativistic BMUE, Table 13 shows that DFT methods perform significantly better than NDO methods and SCC-DFTB for the model Zn model compounds in this study. BMUEs for DFT methods ranged from 0.333 to 1.684,

**Table 13.** Balanced Mean Unsigned Errors (BMUEs, Unitless) for Three Databases of Zn–Ligand Compounds for DFT, HF, and NDO Methods (Nonrelativistic)<sup>a</sup>

functional	BMUE	functional	BMUE
M05-2X	0.333	OVWN5	0.900
B97-2	0.376	OPWL	0.904
mPW1PW	0.426	G96LYP1M	0.909
M05	0.437	G96HLYP	0.912
PW6B95	0.438	G96VWN5	0.953
MPW1B95	0.450	BLYP	1.00
B1LYP	0.451	G96LYP	1.01
PBEh	0.456	mPWLYP	1.02
X3LYP	0.496	mPWVWN5	1.08
B3LYP	0.510	PBELYP	1.09
M06-2X	0.518	PBEVWN5	1.12
TPSS1KCIS	0.535	BVWN5	1.14
M06-L	0.541	HF	1.22
O3LYP	0.542	MOHLYP	1.58
TPSSh	0.550	SVWN5	1.68
M06	0.551	PM3	1.96
$\tau$ -HCTH	0.601	PM6	2.02
MPW1KCIS	0.644	AM1	2.06
TPSS	0.701	MNDO(d)	2.56
VSXC	0.784	MNDO	2.69
OLYP	0.786		
OV5LYP	0.796		
BP86	0.800		
TPSSVWN5	0.885		
MPWLYP1M	0.895		

<sup>a</sup> Nonrelativistic DFT/B1 and other methods tested against nonrelativistic CCSD(T)/B2 for geometries and bond dissociation energies and against nonrelativistic CCSD/B2 for dipole moments.

while NDO methods yielded BMUEs between 1.964 (PM3, best) to 2.686 (MNDO, worst). The HF theory resulted in a BMUE of 1.222, less favorable than all but two of the studied DFT methods. With a BMUE of 1.964, PM3 is the best NDO method; however, PM3 still tested worse than all DFT methods we examined. While SCC-DFTB returned very inaccurate bond dissociation energies (see above) and was therefore not included in the calculations of BMUE, its performance was far better for bond lengths (MUE = 0.043 Å, best among the NDO methods) and somewhat better for dipole moments (MUE = 1.45 D, worst among the NDO methods).

The M05-2X functional,<sup>58</sup> which has demonstrated excellent performance for noncovalent interactions and barrier heights in tests against broad main-group databases<sup>58,122</sup> and tests for silicon chemistry,<sup>123</sup> gives the lowest overall nonrelativistic BMUE (0.333) for this compound set. M05-2X was parametrized against 34 nonmetal data values, whereas the closely related M05 functional was parametrized for metals as well as nonmetals.<sup>57</sup> Interestingly, here we find that M05-2X performs better for Zn than does M05 (nonrelativistic BMUE = 0.437), indicating that Zn, a  $d^{10}$  transition metal, may more closely resemble a main-group element than it does other transition metals. This may also explain the extremely poor performance of the MOHLYP functional, a transition-metal-parametrized GGSC method, with regard to geometries.

**Table 14.** Mean Unsigned Errors in Bond Length (Å) and Dipole Moment (D) with the 6-31+G(d,p) Basis for H, C, N, O, S<sup>a</sup>

bond length	MUE (Å)	dipole moment	MUE (D)
PBEh	0.0068	M05-2X	0.20
PW6B95	0.0068	B97-2	0.23
mPW1PW	0.0073	mPW1PW	0.25
M05-2X	0.0091	M05	0.25
B97-2	0.0094	MPW1B95	0.26
X3LYP	0.0096	PBEh	0.26
MPW1KCIS	0.0096	PW6B95	0.30
M06-L	0.0099	O3LYP	0.32
TPSS1KCIS	0.0102	OVVNS	0.34
TPSSh	0.0103	OPWL	0.34
M06	0.0110	TPSSh	0.34
B3LYP	0.0111	B1LYP	0.34
BP86	0.0112	TPSS1KCIS	0.35
TPSS	0.0118	M06-2X	0.37
B1LYP	0.0120	$\tau$ -HCTH	0.38
M05	0.0133	M06-L	0.39
$\tau$ -HCTH	0.0144	X3LYP	0.40
MPW1B95	0.0145	MOHLYP	0.40
O3LYP	0.0166	B3LYP	0.40
VSXC	0.0181	M06	0.41
M06-2X	0.0194	OV5LYP	0.41
G96LYP	0.0213	OLYP	0.45
MPWLYP1M	0.0218	VSXC	0.51
mPWLYP	0.0248	TPSSVWNS	0.53
HF	0.0248	TPSS	0.53

<sup>a</sup> Otherwise the same as Tables 7 and 9. Only the top 25 functionals are shown for each property.

**Table 15.** Balanced Mean Unsigned Errors (BMUEs, Unitless) for Three Databases of Zn–Ligand Compounds for DFT Methods (Relativistic)<sup>a</sup> and NDO Methods

method	BMUE	method	BMUE
M05-2X	0.414	X3LYP	0.527
B97-2	0.439	B3LYP	0.550
PW6B95	0.444	PM3	1.81
mPW1B95	0.457	AM1	1.84
M05	0.458	PM6	1.91
mPW1PW	0.476	MNDO	2.33
PBEh	0.500	MNDO(d)	2.35
B1LYP	0.504		

<sup>a</sup> Relativistic DFT/B2 and other methods tested against relativistic CCSD(T)/B2 for geometries and bond dissociation energies and against relativistic CCSD/B2 for dipole moments.

Also in the top five functionals tested were B97-2 (BMUE = 0.376), mPW1PW (BMUE = 0.426), M05 (BMUE = 0.437), and PW6B95 (BMUE = 0.438). The popular B3LYP theory ranks #10 overall (BMUE = 0.510), testing quite well for geometries (MUE = 0.008 Å) but less so for dipole moments (MUE = 0.44 D) and bond dissociation energies (MUE = 5.41 kcal/mol).

Inclusion of HF exchange is found to be very helpful for the Zn compounds we included in the present tests: all functionals with HF exchange resulted in nonrelativistic BMUEs below the normalized mean of 1.0, whereas 45% of the functionals with no HF exchange yielded nonrelativistic BMUEs above 1.0. Ten additional functionals with X

= 0 give BMUEs above 0.7: TPSS, OLYP, OV5LYP, VSXC, BP86, TPSSVWN5, OVWN5, OPWL, G96HLYP, and G96VWN5. The best theory level with no HF exchange is M06-L, a new local functional which recently performed best for a broad combination of main-group thermochemistry, thermochemical kinetics, organometallic/inorganometallic, and noncovalent interactions as well as for geometric parameters and vibrational frequencies.<sup>59</sup> Because local functionals are considerably less expensive than nonlocal functionals for large systems, the M06-L local functional has been suggested<sup>59</sup> for calculations involving medium-to-large systems and/or simulations involving longer time scales.

Incorporating the kinetic energy density  $\tau_\sigma$  tended to lower the BMUE. All functionals that include  $\tau_\sigma$  resulted in BMUEs better than the mean, and three of the top five functionals include  $\tau_\sigma$ : M05-2X and M05 in both exchange and correlation and PW6B95 in correlation. However, including  $\tau_\sigma$  does not appear to be a requirement for a good Zn functional; the other two of the top five theory levels do not incorporate it. In general, HMGGA and MGGA methods tested favorably for Zn compounds; GGA, GGE, and GGSC methods were less suitable, and the one LSDA method we evaluated, SVWN5, was the least favorable functional.

For bond lengths and dipole moments, we also carried out complete tests of the same density functionals with the smaller 6-311+G(d,p)<sup>124</sup> basis set for H, C, N, O, and S combined with the Zn basis as used in B1. We found similar trends to the results presented here, and so these results are not presented in detail. However, it is useful to summarize them, and this is done in Table 14, which presents the 25 best methods for geometries and the 25 best methods for dipole moments. For geometries, some methods actually perform better with the smaller basis set, but on average the errors increase by approximately 10%. In contrast the errors in the dipole moments tend to decrease about 10% with the smaller basis. This either indicates that the smaller basis is better balanced or is an encouraging indication that one can achieve similar accuracy with augmented polarized double- $\zeta$  basis sets to what one can obtain with augmented polarized triple- $\zeta$  basis sets. (The performance of augmented polarized double- $\zeta$  basis sets relative to larger basis sets in DFT calculations is also discussed elsewhere.<sup>100</sup>)

**4.2. Relativistic Tests.** One of the key findings of the present study is that scalar relativistic effects are not negligible for Zn compounds. Table 1 shows that when relativistic effects are added, Zn bond lengths all decrease, with an average change of 0.011 Å, which is a factor of 1.7 larger than the smallest mean unsigned error in Table 7. This decrease is as expected, since the direct relativistic effect<sup>125</sup> decreases the size of core *s* and *p* electrons. Table 3 shows that relativistic effects on dipole moments are less systematic, with six dipole moments decreasing by an average of 0.20 D and two increasing by an average of 0.16 D. The Zn–ligand bond energies are also sensitive to relativistic effects; seven of them increase by an average of 4.7 kcal/mol, and the other five decrease by an average of 2.1 kcal/mol. Table 11 shows that these average changes are larger than the mean unsigned errors in the six best functionals.

We considered relativistic effects for the ten density functionals that performed best in the tests (discussed in section 4.1) of nonrelativistic density functional calculations against nonrelativistic best estimates. Relativistic density functional calculations (that is, density functional calculations employing relativistic effective core potentials) were carried out for these ten functionals and were compared to the relativistic best-estimate results. These relativistic tests lead to the same conclusions as the nonrelativistic ones, that is, the functionals that perform well in the nonrelativistic tests also perform well in the relativistic ones. Table 15 shows the performance of DFT and NDO methods against relativistic benchmarks, where both DFT and CCSD(T) calculations incorporate the multielectron-fit (MEFIT,*R*) pseudopotential of Preuss et al. on Zn.<sup>95</sup> M05-2X remains the top functional, with B97-2, PW6B95, mPW1B95, and M05 in second through fifth places, in that order. The kinetic energy density  $\tau_\sigma$  is present in four of these five best performing functionals, and the Hartree–Fock exchange ranges from 21 to 56%.

## 5. Summary and Concluding Remarks

We have presented nonrelativistic and relativistic databases of CCSD(T) geometric parameters and bond dissociation energies and CCSD dipole moments, for a set of Zn model compounds, and used them as benchmarks to test a variety of nonrelativistic and relativistic DFT methods and other molecular orbital methods. While the accuracy of the DFT methods we tested varies considerably, as measured by balanced mean unsigned error (BMUE), DFT overall significantly outperformed NDO (“semiempirical”) and tight-binding molecular orbital methods for our compound sets. Although NDO and tight-binding methods are parametrized against experimental data and therefore include electron correlation effects implicitly, it is disappointing that their overall errors (measured by BMUE against nonrelativistic benchmarks) are factors of 1.5–2.1 larger than *ab initio* Hartree–Fock. Two of the 38 density functionals we tested also fared worse in the nonrelativistic tests than *ab initio* Hartree–Fock. Seventeen density functionals (including five developed in Minnesota), however, have BMUEs more than a factor of 2 lower than HF.

Our results indicate that the suitability of a particular functional for Zn is enhanced by Hartree–Fock (HF) exchange and often, although not necessarily, by including the kinetic energy density  $\tau_\sigma$ . The M05-2X functional has been recommended for general-purpose, nonmetal thermochemistry, kinetics, and noncovalent interactions.<sup>58</sup> Based on our analysis of nonrelativistic and relativistic mean unsigned errors (MUEs), in which M05-2X surpasses all other methods tested, we now recommend it to obtain accurate geometric parameters, dipole moments, and bond dissociation energies for Zn centers. For those interested in a broadly applicable local (*X* = 0) functional with reduced computational cost, perhaps to model larger Zn systems or for simulations of longer duration, we suggest the M06-L and  $\tau$ -HCTH functionals, which display the best performance of the 20 local functionals studied.

Zinc represents an interesting borderline case in the periodic table:<sup>126</sup> it is sometimes considered a transition metal



and sometimes a main-group element. The present study indicates that the computational chemistry requirements of Zn resemble those of the main group rather than the first transition row, as the best functionals for Zn are those that generally perform best for the main group.

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**Supporting Information Available:** Geometries at the X3LYP and M05-2X levels, dipole moments at the M05-2X and B97-2 levels, bond dissociation energies at the M05-2X and M05 levels, mean signed errors for all methods (relativistic/B2 and nonrelativistic/B1), and mean unsigned errors in bond length, dipole moment, and bond dissociation energy (relativistic/B2). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (1) Auld, D. S. In *Handbook on Metalloproteins*; Bertini, I., Sigel, A., Sigel, H., Eds.; Dekker: New York, 2001; p 881.
- (2) Dudev, T.; Lim, C. *Chem. Rev.* **2003**, *103*, 773.
- (3) Silva, J. J. R. F. D.; Williams, R. J. P. *The Biological Chemistry of the Elements: The Inorganic Chemistry of Life*, 2nd ed.; Oxford University Press: New York, 2001.
- (4) Wu, H. Z.; Qiu, D. J.; Cai, Y. J.; Xu, X. L.; Chen, W. B. *J. Cryst. Growth* **2002**, *245*, 50.
- (5) Koca, J.; Zhan, C. G.; Rittenhouse, R. C.; Ornstein, R. L. *J. Comput. Chem.* **2003**, *24*, 368.
- (6) Kikuchi, K.; Komatsu, K.; Nagano, T. *Curr. Opin. Chem. Biol.* **2004**, *8*, 182.
- (7) Remko, M.; Garaj, V. *Mol. Phys.* **2003**, *101*, 2357.
- (8) Porento, M.; Hirva, P. *Theor. Chem. Acc.* **2002**, *107*, 200.
- (9) Dewar, M. J. S.; Merz, K. M., Jr. *Organometallics* **1988**, *7*, 522.
- (10) Onciul, A. R. V.; Clark, T. *J. Comput. Chem.* **1993**, *14*, 392.
- (11) Stanton, R. V.; Merz, K. M., Jr. *J. Chem. Phys.* **1994**, *100*, 434.
- (12) Shoner, S. C.; Humphreys, K. J.; Barnhart, D.; Kovacs, J. A. *Inorg. Chem.* **1995**, *34*, 5933.
- (13) Olson, L. P.; Luo, J.; Almarsson, O.; Bruice, T. C. *Biochemistry* **1996**, *35*, 9782.
- (14) Gresh, N.; Garmer, D. R. *J. Comput. Chem.* **1996**, *17*, 1481.
- (15) Vanhommeig, S. A. M.; Meier, R. J.; Stuyterman, L. A. A.; Meijer, E. M. *Theochem* **1996**, *364*, 33.
- (16) Vaz, R. J.; Kuntz, I. D.; Meng, E. C. *Med. Chem. Res.* **1999**, *9*, 479.
- (17) Amin, E. A.; Welsh, W. J. *J. Med. Chem.* **2001**, *44*, 3849.
- (18) Yazal, J. E.; Pang, Y.-P. *Theochem* **2001**, *545*, 271.
- (19) Elstner, M.; Cui, Q.; Munih, P.; Kaxiras, E.; Frauenheim, T.; Karplus, M. *J. Comput. Chem.* **2003**, *24*, 565.
- (20) Remko, M.; Garaj, V. *Mol. Phys.* **2003**, *101*, 2357.
- (21) Banci, L. *Curr. Opin. Chem. Biol.* **2003**, *7*, 143.
- (22) Asthagiri, D.; Pratt, L. R.; Paulaitis, M. E.; Rempe, S. B. *J. Am. Chem. Soc.* **2004**, *125*, 1285.
- (23) Linder, D. P.; Rodgers, K. R. *J. Phys. Chem. B* **2004**, *108*, 13839.
- (24) Ambroggio, X. I.; Rees, D. C.; Deshaies, R. J. *PLoS Biol.* **2004**, *2*, 113.
- (25) Dudev, T.; Chang, L.-Y.; Lim, C. *J. Am. Chem. Soc.* **2005**, *127*, 4091.
- (26) Martino, T.; Russo, N.; Toscano, M. *J. Am. Chem. Soc.* **2005**, *127*, 4242.
- (27) Sakharov, D. V.; Lim, C. *J. Am. Chem. Soc.* **2005**, *127*, 4921.
- (28) Gresh, N.; Piquemal, J.-P.; Krauss, M. *J. Comput. Chem.* **2005**, *26*, 1113.
- (29) Estiu, G.; Suarez, D.; Merz, K. M., Jr. *J. Comput. Chem.* **2006**, *27*, 1240.
- (30) Sousa, S. F.; Fernandes, P. A.; Ramos, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 1378.
- (31) Yazal, J.E.; Pang, Y.-P. *J. Mol. Struct. Theochem* **2001**, *545*, 271.
- (32) Kornhaber, G. J.; Snyder, D.; Moseley, H. N. B.; Montelione, G. T. *J. Biomol. NMR* **2006**, *34*, 259.
- (33) Xu, D.; Guo, H.; Cui, Q. *J. Phys. Chem. A* **2007**, *111*, 5630.
- (34) Fan, Y.; Gao, Y. Q. *J. Am. Chem. Soc.* **2007**, *129*, 905.
- (35) Bergquist, C.; Fillebeen, T.; Morlok, M.; Parkin, G. *J. Am. Chem. Soc.* **2003**, *125*, 6189.
- (36) Dudutiene, V.; Baranauskienė, L.; Matulis, D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3335.
- (37) Christianson, D. W.; Fierke, C. A. *Acc. Chem. Res.* **1996**, *29*, 331.
- (38) Lavrov, E. V.; Weber, J.; Börrnert, F.; Van de Walle, C. G.; Helbig, R. *Phys. Rev. B* **2002**, *66*, 165205.
- (39) Myong, S. Y.; Park, S. I.; Lim, K. S. *Thin Solid Films* **2006**, *513*, 148.
- (40) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974.
- (41) Zerner, M. C. *Rev. Comp. Chem.* **1991**, *2*, 313.
- (42) *Molecular Orbital Calculations for Biological Systems*; Sapse, A.-M., Ed.; Oxford University Press: New York, 1998.
- (43) Rey, J.; Savin, A. *Int. J. Quantum Chem.* **1998**, *69*, 581.
- (44) Krieger, J. B.; Chen, J.; Iafrate, G. J.; Savin, A. In *Electron Correlations and Materials Properties*; Gonis, A., Kioussis, N., Eds.; Plenum: New York, 1999; p 463.
- (45) Toulouse, J.; Savin, A.; Adamo, C. *J. Chem. Phys.* **2002**, *117*, 10465.
- (46) Tao, J.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. *Phys. Rev. Lett.* **2003**, *91*, 146401.
- (47) Zhao, Y.; Lynch, B. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2005**, *7*, 43.
- (48) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
- (49) Handy, N. C.; Cohen, A. J. *Mol. Phys.* **2001**, *99*, 403.
- (50) Hoe, W.-M.; Cohen, A. J.; Handy, N. C. *Chem. Phys. Lett.* **2001**, *341*, 319.

- (51) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664.
- (52) Zhao, Y.; Gonzalez-Garcia, N.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 1012.
- (53) Staroverov, V. N.; Scuseria, G. E.; Tao, J.; Perdew, J. P. *J. Chem. Phys.* **2003**, *119*, 12129; **2004**, *121*, 11507(E).
- (54) Wilson, P. J.; Bradley, T. J.; Tozer, D. J. *J. Chem. Phys.* **2001**, *115*, 9233.
- (55) Schultz, N. E.; Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 11127.
- (56) Gill, P. M. W. *Mol. Phys.* **1996**, *89*, 433.
- (57) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Phys.* **2005**, *123*, 161103.
- (58) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *2*, 364.
- (59) Zhao, Y.; Truhlar, D. G. *J. Chem. Phys.* **2006**, *125*, 194101.
- (60) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* In press.
- (61) Slater, J. C. *Quantum Theory of Molecules and Solids*; McGraw-Hill: New York, 1974; Vol. 4.
- (62) Vosko, S. H.; Wilk, L.; Nussair, M. *Can. J. Phys.* **1980**, *58*, 1200.
- (63) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822.
- (64) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
- (65) Perdew, J. P. In *Electronic Structure of Solids*; Ziesche, P., Eschrig, H., Eds.; Kademie Verlag: Berlin, 1991; p 11.
- (66) Perdew, J. P.; Wang, Y. *Phys. Rev. B* **1992**, *45*, 13244.
- (67) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
- (68) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.
- (69) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040.
- (70) Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865.
- (71) Adamo, C.; Barone, V. *Chem. Phys. Lett.* **1997**, *274*, 242.
- (72) Voorhis, T. V.; Scuseria, G. E. *J. Chem. Phys.* **1998**, *109*, 400.
- (73) Hamprecht, F. A.; Cohen, A. J.; Tozer, D. J.; Handy, N. C. *J. Chem. Phys.* **1998**, *109*, 6264.
- (74) Adamo, C.; Barone, V. *J. Chem. Phys.* **1999**, *110*, 6158.
- (75) Boese, A. D.; Handy, N. C. *J. Chem. Phys.* **2002**, *116*, 9559.
- (76) Xu, X.; Goddard, W. A. *I. Proc. Natl. Acad. Sci.* **2004**, *101*, 2673.
- (77) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908.
- (78) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 5656.
- (79) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
- (80) Dewar, M. J. S.; Jie, C.; Yu, G. *Tetrahedron* **1993**, *23*, 5003.
- (81) Holder, A. J.; Dennington, R. D.; Jie, C.; Yu, G. *Tetrahedron* **1994**, *50*, 627.
- (82) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.
- (83) Dewar, M. J. S.; Merz, K. M., Jr. *Organometallics* **1986**, *5*, 1494.
- (84) Thiel, W.; Voityuk, A. *Theor. Chim. Acta* **1992**, *81*, 391.
- (85) Thiel, W.; Voityuk, A. A. *J. Phys. Chem.* **1996**, *100*, 616.
- (86) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209.
- (87) Hehre, W. J.; Yu, J.; Adei, E. *Abstracts of Papers*, 212th ACS National Meeting, Orlando, FL, Aug. 25–29, 1996; American Chemical Society: Washington, DC, 1996; COMP 092.
- (88) Hehre, W. J.; Yu, J.; Adei, E. *A Guide of Molecular Mechanics and Molecular Orbital Calculations in SPARTAN*; Wavefunction Inc.: Irvine, CA, 1997.
- (89) Cundari, T. R.; Deng, J. *J. Chem. Inf. Comput. Sci.* **1999**, *39*, 376.
- (90) Bosque, R.; Maseras, F. *J. Comput. Chem.* **2000**, *21*, 562.
- (91) Stewart, J. J. P. *Abstracts of Papers*, 232nd ACS National Meeting, San Francisco, CA, Sept. 10–14, 2006; American Chemical Society: Washington, DC, 2006; COMP 134.
- (92) Porezag, D.; Frauenheim, T.; Köhler, T.; Seifert, G.; Kaschner, R. *Phys. Rev. B* **1995**, *51*, 12947.
- (93) Seifert, G.; Porezag, D.; Frauenheim, T. *Int. J. Quantum Chem.* **1996**, *58*, 185.
- (94) Elstner, M.; Porezag, D.; Jungnickel, G.; Elsner, J.; Haugk, M.; Frauenheim, T.; Suhai, S.; Seifert, G. *Phys. Rev. B* **1998**, *58*, 7260.
- (95) Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. *J. Chem. Phys.* **1987**, *86*, 866.
- (96) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; 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.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, revision D.01*; Gaussian, Inc.: Wallingford, CT, 2004.
- (97) Wachters, A. J. H. *J. Chem. Phys.* **1970**, *52*, 1033.
- (98) Hay, P. J. *J. Chem. Phys.* **1977**, *68*, 4377.
- (99) Raghavachari, K.; Trucks, G. W. *J. Chem. Phys.* **1989**, *91*, 1062.
- (100) Lynch, B. J.; Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2003**, *107*, 1384.
- (101) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.
- (102) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265.
- (103) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.
- (104) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294.

- (105) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1998**, *109*, 7764.
- (106) Federov, D. G.; Koseki, S.; Schmidt, M. W.; Gordon, M. S. *Int. Rev. Phys. Chem.* **2003**, *22*, 551.
- (107) Moore, C. National Bureau of Standard (U.S.) Circular 467, 2952.
- (108) Schultz, N. E.; Gherman, B. F.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2006**, *110*, 24030.
- (109) Shayesteh, A.; Yu, S.; Bernath, P. *Chem. Eur. J.* **2005**, *11*, 4709.
- (110) Shayesteh, A.; Gordon, I.; Appadoo, D.; Bernath, P. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3132.
- (111) Cizek, J. *Adv. Chem. Phys.* **1969**, *14*, 35.
- (112) Bartlett, R. J. *J. Phys. Chem.* **1989**, *93*, 1697.
- (113) Raghavachari, K.; Trucks, G. W.; Pople, J. A.; Head-Gordon, M. *Chem. Phys. Lett.* **1989**, *157*, 479.
- (114) Kinal, A.; Piecuch, P. *J. Phys. Chem. A* **2007**, *111*, 734.
- (115) Wong, B. M.; Raman, S. *J. Comput. Chem.* **2007**, *28*, 759.
- (116) Jurecka, P.; Cerny, J.; Hobza, P.; Salahub, D. R. *J. Comput. Chem.* **2007**, *28*, 555.
- (117) Hill, J. G.; Platt, J. A.; Werner, H. J. *Phys. Chem. Chem. Phys.* **2006**, *125*, 133206.
- (118) Schultz, N. E.; Truhlar, D. G. Unpublished.
- (119) Wavefunction, Inc., Irvine, CA.
- (120) Stewart, J. J. P. <http://mopac2007.net> (accessed February 23, 2007).
- (121) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2006**, *110*, 5121.
- (122) Zheng, J.; Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2007**, in press.
- (123) Zhang, Y.; Li, Z. H.; Truhlar, D. G. *J. Chem. Theory Comput.* **2007**, ASAP.
- (124) Hehre, W. J.; Radom, L.; Schleyer, P. V. R.; Pople, J. A. In *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.
- (125) Rose, S. J.; Grant, I. P.; Pyper, N. J. *J. Phys. B* **1978**, *11*, 1171.
- (126) Mann, J. B.; Meek, T. L.; Allen, L. C. *J. Am. Chem. Soc.* **2000**, *122*, 2780.

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