J. Phys. Chem. A **2001,** *105,* 5356−5371

Calculation of Optical Rotation Using Density Functional Theory

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Received: February 8, 2001; In Final Form: March 23, 2001

We report calculations of the frequency-dependent electric dipole−magnetic dipole polarizability tensor, $\beta_{\alpha\beta}(\nu)$, using ab initio density functional theory (DFT). Gauge invariant (including) atomic orbitals (GIAOs) are used to guarantee origin-independent values of $\beta = (^1/_3)\mathrm{Tr}\,[\beta_{\alpha\beta}]$. Calculations of β at the sodium D line frequency, β(D), for 30 rigid chiral molecules are used to predict their specific rotations, $[\alpha]_D$. Calculations have been carried out using the B3LYP functional and the 6-31G*, DZP, 6-311++G(2d,2p), aug-cc-pVDZ, and aug-cc-pVTZ basis sets. Comparison to experimental $[\alpha]_D$ values for 28 of the 30 molecules yields average absolute deviations of calculated and experimental $[\alpha]_D$ values in the range 20−25° for the three large basis sets, all of which include diffuse functions. The accuracies of $[\alpha]_D$ values calculated using the 6-31G* and DZP basis sets, which do not include diffuse functions, are significantly lower: average deviations from experiment are 33° and 43°, respectively. Hartree−Fock/Self-Consistent Field (HF/SCF) calculations have been carried out in parallel. HF/SCF $[\alpha]_D$ values are substantially lower in accuracy than corresponding B3LYP values; at the aug-cc-pVDZ basis set level, the average deviation from experiment is 63°. $[\alpha]_D$ values obtained using β values calculated in the static limit ($\nu = 0$) are also of lower accuracy than values obtained using β(D). Absolute Configurations of chiral molecules can be assigned by comparison of predicted and experimental optical rotations. Our results demonstrate that DFT provides substantially more accurate rotations than HF/SCF methodologies employed heretofore and therefore constitutes the current method of choice for stereochemical applications.

Introduction

The optical rotation at frequency ν of an isotropic dilute solution of a chiral molecule can be written

$$\phi(\nu) = \sum_{x} \alpha_x \sum_{c} \alpha_c\, \phi\,(X, C, \nu) \tag{1}$$

where $\phi(X, C, \nu)$ is the rotation of the molecule in conformation C and Absolute Configuration (AC) X. α_c is the fraction of molecules in conformation C: $\sum\alpha_c = 1$. α_x is the fraction of molecules in AC X. Labeling the two ACs X_1 and X_2, $\alpha_{x1} + \alpha_{x2} = 1$. If $\alpha_{x1} > \alpha_{x2}$, the enantiomeric excess (ee) of X_1 is ee $(X_1) = 100\,(\alpha_{x1} - \alpha_{x2})$. Enantiomers exhibit optical rotation of opposite sign and equal magnitude: $\phi(X_1, C, \nu) = -\phi\,(X_2, C, \nu)$. Hence, if X_1 is the dominant enantiomer

$$\phi(\nu) = \frac{\mathrm{ee}(X_1)}{100} \sum_{c} \alpha_c\, \phi(X_1, C, \nu) \tag{2}$$

The theoretical prediction of optical rotation thus requires α_c and $\phi(X_1, C, \nu)$ for all significantly populated conformations, together with ee (X_1). The ee must be determined experimentally for the specific sample. The parameters to be predicted theoretically are thus α_c and $\phi(X_1, C, \nu)$.

In this paper, we address the calculation of $\phi(X_1, C, \nu)$. Specifically, we evaluate a new methodology for the calculation of $\phi(X_1, C, \nu)$ based on ab initio Density Functional Theory (DFT).[1] In order to assess the accuracy of this methodology, we have carried out calculations for a large number of molecules, all of which are "rigid" i.e., they exhibit only one conformation. In this case eq 2 reduces to

$$\phi(\nu) = \frac{\mathrm{ee}(X_1)}{100}\, \phi(X_1, \nu) \tag{3}$$

and the complications of conformational flexibility are avoided.

The fundamental equation for $\phi(X_1, \nu)$ in radians/cm is[2]

$$\phi(X_1, \nu) = \frac{16\pi^3 N \nu^2}{c^2}\, \gamma_s\, \langle(\beta\,(X_1,\nu)\rangle_v \tag{4}$$

where N is the number of molecules/cm^3, γ_s is the solvent effect and

$$\beta(X_1, \nu) = \frac{1}{3}\,\mathrm{Tr}\,[\beta_{\alpha\beta}\,(X_1, \nu)] \tag{5}$$

$\beta_{\alpha\beta}(\nu)$ is the frequency-dependent electric dipole−magnetic dipole polarizability (also referred to as $-[(^{c}/_{2\pi\nu})\,G'_{\alpha\beta}]$[3]), given by

$$\beta_{\alpha\beta}\,(\nu) = \frac{c}{3\pi h}\,\mathrm{Im}\left[\sum_{k\neq 0} \frac{\langle 0|(\mu^{e}_{el})_{\alpha}|k\rangle\langle k|(\mu^{e}_{mag})_{\beta}|0\rangle}{\nu_{k0}^2 - \nu^2}\right] \tag{6}$$

where 0 and k label ground and excited electronic states and $\vec{\mu}^{\,e}_{el}$ and $\vec{\mu}^{\,e}_{mag}$ are the electronic electric dipole and magnetic dipole operators, respectively. Equation 6 assumes that $\nu \ll \nu_{ko}$

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10.1021/jp0105138 CCC: $20.00

for all k; when this is not the case, damping must be included. In eq 4 $\langle\ \rangle_v$ indicates vibrational averaging of β. We can write

$$\langle\beta(\nu)\rangle_v = \gamma_v\,[\beta(\nu)]_o \tag{7}$$

where $[\beta(\nu)]_0$ is the value of $\beta(\nu)$ at the equilibrium geometry of the molecule. Then

$$\phi(X_1,\nu) = \frac{16\pi^3 N\nu^2}{c^2}\,\gamma_s\gamma_v[\beta(X_1,\,\nu)]_o \tag{8}$$

Prediction of $\phi(X_1,\ \nu)$ thus requires calculation of $[\beta(X_1,\ \nu)]_0$, γ_v, and γ_s. In this paper, we focus on the calculation of $[\beta(X_1,\ \nu)]_0$.

The calculation of $\beta_{\alpha\beta}$ using ab initio methods was first implemented by Amos.[4] The implementation was restricted to the zero-frequency (static) limit, when

$$\beta_{\alpha\beta}\,(0) = \frac{hc}{3\pi}\,\mathrm{Im}\left[\left\langle\left(\frac{\partial\psi_0}{\partial E_\alpha}\right)_0\middle|\left(\frac{\partial\psi_0}{\partial H_\beta}\right)_0\right\rangle\right] \tag{9}$$

$\partial\psi_o/\partial E_\alpha$ and $\partial\psi_o/\partial H_\beta$ are the derivatives of the ground-state electronic wave function with respect to E_α and H_β in the presence of the perturbations $-(\mu^e_{el})_\alpha E_\alpha$ and $-(\mu^e_{mag})_\beta H_\beta$ respectively. $\partial\psi_o/\partial E_\alpha$ and $\partial\psi_o/\partial H_\beta$ were calculated at the Hartree–Fock (HF)/Self-Consistent Field (SCF) level using analytical derivative methods and field-independent atomic orbitals (FIAOs). Subsequently, Helgaker et al.[5] used HF/SCF linear response methods to calculate $\beta_{\alpha\beta}$ without restriction to the static limit and using either FIAOs or Gauge-Invariant (Including) Atomic Orbitals (GIAOs) (also referred to as London orbitals).[6]

Amos and Helgaker et al. did not use their respective methodologies to calculate optical rotations. However, in the last few years, Polavarapu et al.[7] and Kondru et al.[8] have reported calculations of optical rotations using both the CADPAC program,[9] which incorporates the methodology of Amos, and the DALTON program[10] which incorporates the methodology of Helgaker et al. Calculations have been carried out with small basis sets, most commonly 6-31G* and DZP. Both rigid and flexible molecules have been studied. For three molecules, an indoline,[8c] an indolinone,[8d] and the natural product pitiamide A,[8e] predicted rotations have been used to assign Absolute Configurations.

The accuracies of optical rotations calculated using the methodologies of Amos and Helgaker et al. are limited by their use of the HF/SCF methodology, in which (by definition) electron correlation is neglected. In this paper, we discuss the application of the DFT methodology to the calculation of optical rotation. Using state of the art functionals, DFT currently provides more accurate results for a wide range of molecular properties than the HF/SCF methodology.[11] It is reasonable to anticipate that this will also hold true for optical rotations. In a recent publication[12] we reported calculations of $\beta_{\alpha\beta}(0)$ and, thence, sodium D line specific rotations, $[\alpha]_D$, using DFT for two molecules. Here we report calculations of $\beta_{\alpha\beta}$ at the sodium D line frequency, $\beta_{\alpha\beta}(D)$, and thence, $[\alpha]_D$, for a much wider range of molecules.

In our application of DFT to the calculation of optical rotation, we use GIAO basis sets. As we have recently emphasized,[12] the choice of FIAOs or GIAOs has important consequences for the origin dependence of $\beta_{\alpha\beta}$. The components of the exact $\beta_{\alpha\beta}$ tensor are origin-dependent; in contrast, β is origin-independent, an obviously necessary requirement for a molecular property directly related to an experimental observable. However, approximate calculations do not necessarily yield origin-independent values of β. When FIAOs are used, β is origin-dependent. The origin-dependence decreases with increasing basis set size and becomes zero in the complete basis set limit. When GIAOs are used, β is origin-independent, irrespective of basis set size. Clearly, only origin-independent calculations can be meaningfully compared to experiment. The use of GIAOs is mandatory, therefore.

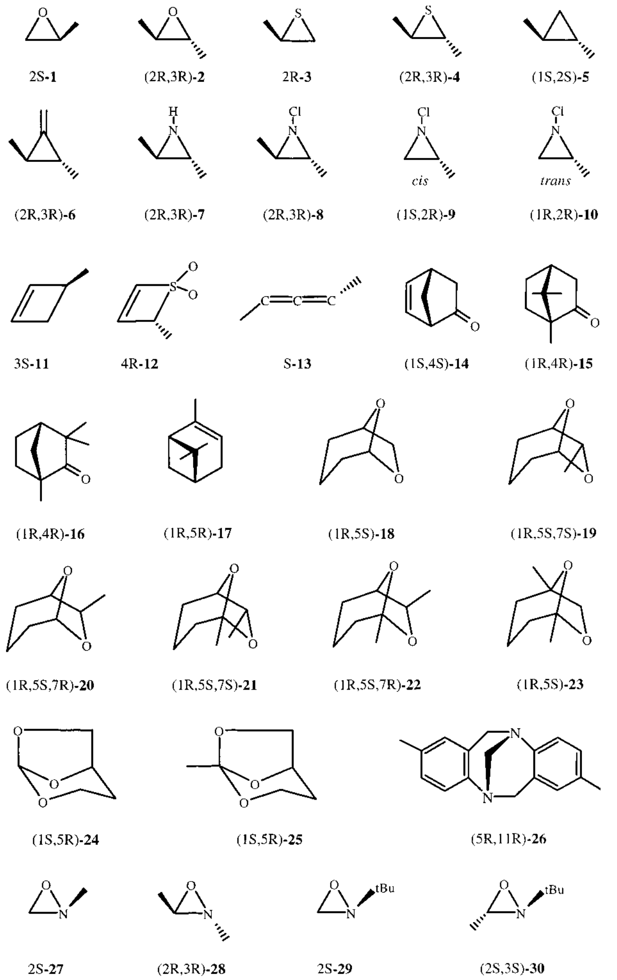
2S-1 (2R,3R)-2 2R-3 (2R,3R)-4 (1S,2S)-5
(2R,3R)-6 (2R,3R)-7 (2R,3R)-8 (1S,2R)-9 (1R,2R)-10
3S-11 4R-12 S-13 (1S,4S)-14 (1R,4R)-15
(1R,4R)-16 (1R,5R)-17 (1R,5S)-18 (1R,5S,7S)-19
(1R,5S,7R)-20 (1R,5S,7S)-21 (1R,5S,7R)-22 (1R,5S)-23
(1S,5R)-24 (1S,5R)-25 (5R,11R)-26
2S-27 (2R,3R)-28 2S-29 (2S,3S)-30

Figure 1. Molecules **1**–**30**. The absolute configurations are those for which ab initio optical rotation calculations were carried out (see Tables 2 and 4).

In characterizing the accuracy of the DFT methodology in calculating optical rotations, it is important to use a large and diverse set of molecules, so that meaningful statistics can be obtained. For this study, we have selected 28 rigid molecules whose specific rotations at the sodium D line frequency have been reported. A large fraction are molecules previously studied by Polavarapu et al.[7] or Kondru et al.[8] To these we have added two for which experimental rotations are not known, also studied by Polavarapu et al.[7e] The 30 molecules **1**–**30**, are detailed in Figure 1. Their optical rotations are listed in Table 1.

DFT optical rotations have been calculated for **1**–**30** using three large basis sets, aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p), and two small basis sets, 6-31G* and DZP. In our recent study of the basis set dependence of optical rotations obtained from DFT and HF/SCF calculations for two molecules, **1** and **4**, we showed that large basis sets incorporating diffuse functions are required to obtain results satisfactorily approximating complete basis set results.[12] The basis set aug-cc-pVTZ is a very large basis set containing diffuse functions. The aug-cc-pVDZ and 6-311++G(2d,2p) basis sets, also

TABLE 1: Experimental Specific Rotations

molecule	AC	$[\alpha]_D$[a]	t[b]	c[c]	solvent	ee[d]	footnote
1	2R	18.7		5	CCl_4		*e*
2	2S, 3S	−58.8	25	-	neat	>99.9	*f*
3	2S	−51.2	10	-	neat		*g*
4	2S, 3S	−129.0	25	-	neat		*h*
5	1R, 2R	−42	25	0.5	*n*-pentane		*i*
6	2S, 3S	−57.6	22	1.72	CCl_4		*j*
7	2S, 3S	−103.8	25	0.2218	*n*-heptane		*k*
8	2S, 3S	16.8	20	3.2	*n*-heptane		*l*
9	1R, 2S	−78.2[z]	20	3.3	*n*-heptane		*m*
10	1S, 2S	103.4[z]	20	3	*n*-heptane		*m*
11	3R	≤175.6	18	-	neat	>66.2	*n*
12	4R	−21.2	21.5	5.995	$CHCl_3$		*o*
13	S	81.0[z]	25	1.250; 0.915	ether	25.9; 47.9	*p*
14	1S, 4S	−1146	25	0.17	hexane	48	*q*
15	1R, 4R	44.1	25	10	C_2H_5OH		*r*
16	1R,4R	−50.5	24	-	neat		*s*
17	1R	51.6	20	-	neat	100	*t*
18	1S, 5R	−115.0	23−25	0.41	*n*-hexane		*u*
19	1R, 5S, 7S	108.1			CCl_4	99	*v*
20	1S, 5R, 7S	−94.4			CCl_4	99	*v*
21	1R, 5S, 7S	86.5			$CHCl_3$	100	*v*
22	1S, 5R, 7S	−66.3			$CHCl_3$	99	*v*
23	1R,5S	56.9	22	4.5	ether	95	*v*
24	1R, 5S	−175.8	27	9.32	toluene		*w*
25	1R, 5S	−139.2	22	9.71	toluene		*w*
26	5S, 11S	287	25	0.29	*n*-hexane		*x*
29	2S	−34.5	27	5%	CCl_4	6	*y*
30	2S, 3S	−37.1	27	-	neat	14	*y*

[a] In degrees $[dm(g/cm^3)]^{-1}$. When ee is measured $[\alpha]_D$ is normalized to 100% ee; otherwise, $[\alpha]_D$ is as reported. [b] °C. [c] g/100 mL. [d] ee of sample whose $[\alpha]_D$ was measured. [e] Ref 23. [f] Schurig, V.; Koppenhoefer, B.; Buerkle, W. *J. Org. Chem.* **1980**, *45*, 538. [g] Tsunetsugu, T.; Furukawa, J.; Fueno, T. *J. Poly. Sci. A-1* **1971**, *9*, 3529. [h] Helmkamp, G. K.; Schnautz, N. *Tetrahedron* **1958**, *2*, 304. [i] Moore, W. R.; Anderson, H. W.; Clark, S. D.; Ozretich, T. M. *J. Am. Chem. Soc.* **1971**, *93*, 4932. [j] Gajewski, J. J. *J. Am. Chem. Soc.* **1971**, *93*, 4450. [k] Dickey, F. H.; Fickett, W.; Lucas, H. J. *J. Am. Chem. Soc.* **1952**, *74*, 944. [l] Shustov, G. V.; Kachanov, A. V.; Korneev, V. A.; Kostyanovsky, R. G.; Rauk, A. *J. Am. Chem. Soc.* **1993**, *115*, 10 267. [m] Shustov, G. V.; Kadorkina, G. K.; Kostyanovsky, R. G.; Rauk, A. *J. Am. Chem. Soc.* **1988**, *110*, 1719. [n] Rossi, R.; Diversi, P. *Tetrahedron* **1970**, *26*, 5033. [o] Paquette, L. A.; Freeman, J. P. *J. Org. Chem.* **1970**, *35*, 2249. [p] Pasto, D. J.; Sugi, K. D. *J. Org. Chem.* **1991**, *56*, 4157. [q] Lightner, D. A.; Gawronski, J. K.; Bouman, T. D. *J. Am. Chem. Soc.* **1980**, *102*, 5749. [r] Aldrich Catalog. [s] Aldrich Catalog. [t] Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Org. Chem.* **1982**, *47*, 4583. [u] Pecka, J.; Cerny, M. *Collect. Czech. Chem. Commun.* **1973,** *38*, 132. [v] Ibrahim, N.; Eggimann, T.; Dixon, E. A.; Weiser, H. *Tetrahedron* **1990,** *46*, 1503; Eggimann, T. Ph.D. Thesis, University of Calgary, Alberta, Canada, 1991. [w] Wroblewski, A. E.; Applequist, J.; Takaya, A.; Honzatko, R.; Kim, S. S.; Jacobson, R. A.; Reitsma, B. H.; Yeung, E. S.; Verkade, J. G. *J. Am. Chem. Soc.* **1988**, *110*, 4144. [x] Wilen, S. C., Qi, J. Z., Williard, P. G., *J. Org. Chem.* **1991**, *56*, 485. [y] Pirkle, W. H., Rinaldi, P. L., *J. Org. Chem.* **1977**, *42*, 3217; Pirkle, W. H., Rinaldi, P. L., *J. Org. Chem.* **1978**, *43*, 4475. [z] Note that older, very different $[\alpha]_D$ values for **9**, **10** and **13** were listed by Polaravapu and co-workers;[7c,7d] **9**: −81; **10**: 94; **13**: 227.

containing diffuse functions, are considerably smaller, but gave results for **1** and **4** close to those given by aug-cc-pVTZ. The small basis sets 6-31G* and DZP, which do not contain diffuse functions, have been the basis sets predominantly used by Polavarapu et al.[7] and Kondru et al.[8] We seek to define their accuracy relative to the much larger basis sets, containing diffuse functions.

We have also carried out parallel calculations using the HF/SCF methodology in order to define its accuracy relative to the DFT methodology.

Results for molecules **18**−**23** have been presented in a prior communication.[13]

Methods

HF/SCF and DFT calculations of $\beta_{\alpha\beta}(\nu)$ are carried out using the time-dependent Hartree−Fock and time-dependent DFT methodologies.[14] In DFT calculations, the adiabatic approximation,[14d] where the exchange-correlation functional is approximated by the exchange-correlation functional of time-independent DFT, has been adopted. The methods used in solving the time-dependent coupled-perturbed Hartree−Fock (CPHF) and Kohn−Sham(CPKS) equations are described in detail elsewhere.[1e] All calculations were performed using direct, analytical derivative methods, implemented within the development version of GAUSSIAN.[15] As discussed previously,[12] origin-independence of $\beta = (^1/_3)\mathrm{Tr}[\beta_{\alpha\beta}]$ is ensured by the use of GIAOs.[6] Calculations have been carried out using five basis sets: aug-cc-pVTZ,[16] aug-cc-pVDZ,[16] 6-311++G(2d,2p),[17] DZP,[18] and 6-31G*.[19] The B3LYP functional[20] has been used in all DFT calculations. All calculations have been carried out at B3LYP/6-31G* geometries.

Values of β have been calculated at the sodium D line frequency and at zero frequency, $\beta(\mathrm{D})$ and $\beta(0)$ respectively, and converted to sodium D line specific rotations $[\alpha]_D$ using[13]

$$[\alpha]_D = \frac{28\,800\pi^2 N_A \nu^2}{c^2 M}\gamma_s\beta \tag{10}$$

where N_A is Avogadro's Number, and M is the molecular weight. The solvent correction is either neglected ($\gamma_s = 1$) or approximated by the Lorentz expression: $\gamma_s = (n^2 + 2)/3$.[2b]

Results

Values of $\beta(\mathrm{D})$, and of $[\alpha]_D$ derived thence neglecting solvent effects (i.e., with $\gamma_s = 1$), obtained using the B3LYP functional and the three large basis sets, aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p) are given in Table 2. Calculations were carried out using aug-cc-pVDZ and 6-311++G(2d,2p) for the 30 molecules **1**−**30** and using aug-cc-pVTZ for the 23 molecules

TABLE 2: Large Basis Set Values of β and $[\alpha]_D$[a]

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	$[\alpha]_D$ (Lorentz)[c]	expt[d]
1	(2S)							−18.7
		B3LYP/						
		aug-cc-pVTZ:	−0.0230	−0.0154	−15.28	−10.26		
		aug-cc-pVDZ:	−0.0338	−0.0263	−22.53	−17.50	−24.10	
		6-311++G(2d,2p):	−0.0277	−0.0196	−18.42	−13.02		
		HF/						
		aug-cc-pVDZ:	−0.0228	−0.0207	−15.18	−13.77		
2	(2R,3R)							58.8
		B3LYP/						
		aug-cc-pVTZ:	0.1266	0.1213	67.92	65.06		
		aug-cc-pVDZ:	0.1509	0.1466	80.91	78.61	101.8	
		6-311++G(2d,2p):	0.1189	0.1117	63.75	59.89		
		HF/						
		aug-cc-pVDZ:	0.1005	0.0995	53.90	53.38		
3	(2R)							51.2
		B3LYP/						
		aug-cc-pVTZ:	0.0736	0.0536	38.37	27.95		
		aug-cc-pVDZ:	0.1172	0.1018	61.13	53.11	73.98	
		6-311++G(2d,2p):	0.1163	0.0998	60.67	52.07		
		HF/						
		aug-cc-pVDZ:	0.1378	0.1503	71.88	78.38		
4	(2R,3R)							129.0
		B3LYP/						
		aug-cc-pVTZ:	0.3076	0.3135	134.94	137.49		
		aug-cc-pVDZ:	0.3670	0.3810	160.98	167.11	229.94	
		6-311++G(2d,2p):	0.3560	0.3625	156.15	158.99		
		HF/						
		aug-cc-pVDZ:	0.3402	0.3713	149.22	162.87		
5	(1S,2S)							42
		B3LYP/						
		aug-cc-pVTZ:	0.0981	0.0976	54.09	53.81		
		aug-cc-pVDZ:	0.1068	0.1070	58.89	58.99	75.57	
		6-311++G(2d,2p):	0.0856	0.0850	47.21	46.84		
		HF/						
		aug-cc-pVDZ:	0.0849	0.0882	46.81	48.63		
6	(2R,3R)							57.6
		B3LYP/						
		aug-cc-pVTZ:	−0.0149	−0.0195	−7.00	−9.19		
		aug-cc-pVDZ:	0.0081	0.0072	3.80	3.40	4.68	
		6-311++G(2d,2p):	−0.0186	−0.0244	−8.74	−11.49		
		HF/						
		aug-cc-pVDZ:	−0.0391	−0.0458	−18.40	−21.58		
7	(2R,3R)							103.8
		B3LYP/						
		aug-cc-pVTZ:	0.1613	0.1754	87.73	95.38		
		aug-cc-pVDZ:	0.1739	0.1895	94.54	103.06	134.80	
		6-311++G(2d,2p):	0.1676	0.1810	91.14	98.41		
		HF/						
		aug-cc-pVDZ:	0.1153	0.1212	62.69	65.93		
8	(2R,3R)							−16.8
		B3LYP/						
		aug-cc-pVTZ:	−0.1009	−0.0907	−36.96	−33.22		
		aug-cc-pVDZ:	−0.0879	−0.0775	−32.21	−28.38	−37.12	
		6-311++G(2d,2p):	−0.0807	−0.0650	−29.58	−23.81		
		HF/						
		aug-cc-pVDZ:	−0.1562	−0.1649	−57.23	−60.42		
9	(1S,2R)							78.2
		B3LYP/						
		aug-cc-pVTZ:	0.1507	0.1800	63.66	76.03		
		aug-cc-pVDZ:	0.1565	0.1859	66.10	78.55	102.74	
		6-311++G(2d,2p):	0.1238	0.1550	52.32	65.47		
		HF/						
		aug-cc-pVDZ:	0.0885	0.1012	37.39	42.76		
10	(1R,2R)							−103.4
		B3LYP/						
		aug-cc-pVTZ:	−0.3062	−0.3229	−129.38	−136.41		
		aug-cc-pVDZ:	−0.2983	−0.3152	−126.01	−133.15	−174.16	
		6-311++G(2d,2p):	−0.2443	−0.2556	−103.23	−107.97		
		HF/						
		aug-cc-pVDZ:	−0.2935	−0.3155	−123.99	−133.27		

TABLE 2: (Continued)

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	$[\alpha]_D$ (Lorentz)[c]	expt[d]
11	(3S)							≤ −175.6
		B3LYP/						
		aug-cc-pVTZ:	−0.2499	−0.2873	−141.87	−163.11		
		aug-cc-pVDZ:	−0.2642	−0.3025	−149.98	−171.73	−226.17	
		6-311++G(2d,2p):	−0.2565	−0.2937	−145.62	−166.74		
		HF/						
		aug-cc-pVDZ:	−0.2005	−0.2276	−113.82	−129.24		
12	(4R)							−21.2
		B3LYP/						
		aug-cc-pVTZ:	−0.1326	−0.1344	−43.40	−44.00		
		aug-cc-pVDZ:	−0.1400	−0.1406	−45.81	−46.03	−62.78	
		6-311++G(2d,2p):	−0.1417	−0.1421	−46.37	−46.52		
		HF/						
		aug-cc-pVDZ:	−0.1016	−0.1076	−33.25	−35.20		
13	(S)							81.0
		B3LYP/						
		aug-cc-pVTZ:	0.2352	0.2425	133.54	137.68		
		aug-cc-pVDZ:	0.2320	0.2385	131.69	135.38	172.88	
		6-311++G(2d,2p):	0.2012	0.2067	114.21	117.32		
		HF/						
		aug-cc-pVDZ:	0.1944	0.2068	110.35	117.38		
14	(1S,4S)							−1146
		B3LYP/						
		aug-cc-pVTZ:	−2.1842	−3.3420	−781.12	−1195.15		
		aug-cc-pVDZ:	−2.2176	−3.3996	−793.03	−1215.76	−1576.84	
		6-311++G(2d,2p):	−2.2204	−3.3847	−794.06	−1210.43		
		HF/						
		aug-cc-pVDZ:	−1.2788	−1.6965	−457.31	−606.69		
15	(1R,4R)							44.1
		B3LYP/						
		aug-cc-pVTZ:	0.1433	0.2365	36.39	60.08		
		aug-cc-pVDZ:	0.1415	0.2388	35.95	60.66	77.83	
		6-311++G(2d,2p):	0.1273	0.2211	32.34	56.16		
		HF/						
		aug-cc-pVDZ:	0.0257	0.0410	6.52	10.41		
16	(1R,4R)							−50.5
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	−0.2037	−0.2652	−51.75	−67.37	−92.90	
		6-311++G(2d,2p):	−0.2096	−0.2721	−53.24	−69.11		
		HF/						
		aug-cc-pVDZ:	−0.1512	−0.1859	−38.41	−47.22		
17	(1R)							51.6
		B3LYP/						
		aug-cc-pVTZ:	0.1428	0.1458	40.53	41.39		
		aug-cc-pVDZ:	0.1455	0.1477	41.31	41.93	57.99	
		6-311++G(2d,2p):	0.1275	0.1305	36.19	37.03		
		HF/						
		aug-cc-pVDZ:	0.1917	0.2193	54.43	62.25		
18	(1R,5S)							115.0
		B3LYP/						
		aug-cc-pVTZ:	0.2514	0.2687	85.19	91.05		
		aug-cc-pVDZ:	0.2604	0.2782	88.22	94.25	122.24	
		6-311++G(2d,2p):	0.2565	0.2744	86.91	92.96		
		HF/						
		aug-cc-pVDZ:	0.1888	0.2002	63.98	67.84		
19	(1R,5S,7S)							108.1
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	0.3406	0.3919	102.78	118.26	162.84	
		6-311++G(2d,2p):	0.3412	0.3922	102.95	118.34		
		HF/						
		aug-cc-pVDZ:	0.1869	0.2026	56.40	61.13		
20	(1R,5S,7R)							94.4
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	0.2728	0.2755	82.31	83.11	114.44	
		6-311++G(2d,2p):	0.2827	0.2862	85.31	86.35		
		HF/						
		aug-cc-pVDZ:	0.2315	0.2400	69.84	72.42		

TABLE 2: (Continued)

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	$[\alpha]_D$ (Lorentz)[c]	expt[d]
21	(1R,5S,7S)							86.5
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	0.2635	0.2974	71.66	80.89	110.33	
		6-311++G(2d,2p):	0.2636	0.2973	71.70	80.85		
		HF/						
		aug-cc-pVDZ:	0.1567	0.1697	42.62	46.14		
22	(1R,5S,7R)							66.3
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	0.1647	0.1578	44.79	42.92	58.54	
		6-311++G(2d,2p):	0.1792	0.1739	48.73	47.29		
		HF/						
		aug-cc-pVDZ:	0.1623	0.1682	44.15	45.73		
23	(1R,5S)							56.9
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	0.1023	0.1044	27.83	28.40	36.27	
		6-311++G(2d,2p):	0.1077	0.1108	29.30	30.13		
		HF/						
		aug-cc-pVDZ:	0.0876	0.0923	23.84	25.10		
24	(1S,5R)							175.8
		B3LYP/						
		aug-cc-pVTZ:	0.3900	0.4318	129.89	143.80		
		aug-cc-pVDZ:	0.4038	0.4475	134.49	149.03	210.58	
		6-311++G(2d,2p):	0.3886	0.4319	129.41	143.84		
		HF/						
		aug-cc-pVDZ:	0.2490	0.2663	82.94	88.68		
25	(1S,5R)							139.2
		B3LYP/						
		aug-cc-pVTZ:	0.3197	0.3586	95.01	106.55		
		aug-cc-pVDZ:	0.3322	0.3728	98.72	110.78	156.53	
		6-311++G(2d,2p):	0.3231	0.3635	96.01	108.01		
		HF/						
		aug-cc-pVDZ:	0.1941	0.2097	57.69	62.31		
26	(5R,11R)							−287
		B3LYP/						
		aug-cc-pVTZ:						
		aug-cc-pVDZ:	−1.5683	−2.2108	−242.26	−341.51	−442.94	
		6-311++G(2d,2p):	−1.4513	−2.0702	−224.20	−319.80		
		HF/						
		aug-cc-pVDZ:	0.0249	0.0323	3.85	4.99		
27	(2S)							
		B3LYP/						
		aug-cc-pVTZ:	−0.1661	−0.1824	−108.73	−119.39		
		aug-cc-pVDZ:	−0.1790	−0.1964	−117.17	−128.60		
		6-311++G(2d,2p):	−0.1731	−0.1901	−113.36	−124.47		
		HF/						
		aug-cc-pVDZ:	−0.2116	−0.2313	−138.54	−151.41		
28	(2R,3R)							
		B3LYP/						
		aug-cc-pVTZ:	0.3168	0.3437	167.61	181.82		
		aug-cc-pVDZ:	0.3361	0.3652	177.84	193.23		
		6-311++G(2d,2p):	0.3469	0.3757	183.52	198.77		
		HF/						
		aug-cc-pVDZ:	0.3281	0.3527	173.57	186.58		
29	(2S)							−34.5
		B3LYP/						
		aug-cc-pVTZ:	−0.0460	−0.0373	−17.59	−14.27		
		aug-cc-pVDZ:	−0.0513	−0.0427	−19.61	−16.32	−22.47	
		6-311++G(2d,2p):	−0.0419	−0.0327	−16.01	−12.50		
		HF/						
		aug-cc-pVDZ:	−0.1499	−0.1614	−57.32	−61.71		
30	(2S,3S)							−37.1
		B3LYP/						
		aug-cc-pVTZ:	−0.2492	−0.2567	−83.68	−86.18		
		aug-cc-pVDZ:	−0.2488	−0.2561	−83.53	−85.98		
		6-311++G(2d,2p):	−0.2602	−0.2677	−87.36	−89.88		
		HF/						
		aug-cc-pVDZ:	−0.3109	−0.3316	−104.38	−111.33		

[a] Values of β are in atomic units; values of $[\alpha]_D$ are in deg[dm·(gm/cc)]$^{-1}$. $\beta(0)$ and $\beta(D)$ are calculated at the static limit, $\nu = 0$, and at the sodium D line frequency, respectively. $[\alpha]_D(0)$ and $[\alpha]_D$ are obtained using $\beta(0)$ and $\beta(D)$ respectively. $[\alpha]_D(0)$ and $[\alpha]_D$ values assume $\gamma_s = 1$ (see text). $[\alpha]_D$ (Lorentz) values are obtained using $\gamma_s = (n^2_D + 2)/3$. [b] See Figure 1. [c] n_D values are from the Aldrich Catalog except for #4 (from Helmkamp, G. K.; Schnautz, N. *Tetrahedron* **1958**, *2*, 304) and #11 (from Rossi, R.; Diversi, P. *Tetrahedron* **1970**, *26*, 5033). [d] From Table 1.

TABLE 3: Mean Absolute Deviations of $[\alpha]_D$ (X) and $[\alpha]_D$ (Y)[a]

X	Y	mean abs	mean abs[b]
B3LYP/aug-cc-pVTZ	B3LYP/aug-cc-pVDZ	7.9	7.3
B3LYP/aug-cc-pVTZ	B3LYP/6-311++G(2d,2p)	8.5	8.2
B3LYP/aug-cc-pVDZ	B3LYP/6-311++G(2d,2p)	6.8	6.3
experiment	B3LYP/aug-cc-pVTZ	24.3	23.0
experiment	B3LYP/aug-cc-pVDZ	23.1	20.1
experiment	B3LYP/6-311++G(2d,2p)	20.8	18.7
B3LYP/aug-cc-pVDZ	HF/aug-cc-pVDZ	55.4	25.2
experiment	HF/aug-cc-pVDZ	62.7	35.5
B3LYP/aug-cc-pVTZ	B3LYP/6-31G*	30.8	24.9
B3LYP/aug-cc-pVTZ	B3LYP/DZP	36.3	36.3
B3LYP/aug-cc-pVDZ	B3LYP/6-31G*	34.3	23.0
B3LYP/aug-cc-pVDZ	B3LYP/DZP	33.2	32.4
B3LYP/6-311++G(2d,2p)	B3LYP/6-31G*	31.1	20.5
B3LYP/6-311++G(2d,2p)	B3LYP/DZP	32.0	32.0
B3LYP/6-31G*	B3LYP/DZP	48.0	40.8
experiment	B3LYP/6-31G*	33.1	25.6
experiment	B3LYP/DZP	42.9	44.8
B3LYP/aug-cc-pVTZ	HF/6-31G*	58.9	32.0
B3LYP/aug-cc-pVTZ	HF/DZP	65.6	41.8
B3LYP/aug-cc-pVDZ	HF/6-31G*	67.1	30.3
B3LYP/aug-cc-pVDZ	HF/DZP	68.2	37.5
B3LYP/6-311++G(2d,2p)	HF/6-31G*	62.6	26.5
B3LYP/6-311++G(2d,2p)	HF/DZP	68.1	38.3
HF/aug-cc-pVDZ	HF/6-31G*	20.7	14.8
HF/aug-cc-pVDZ	HF/DZP	22.3	22.5
B3LYP/6-31G*	HF/6-31G*	45.1	20.5
B3LYP/DZP	HF/DZP	52.8	24.2
HF/6-31G*	HF/DZP	31.4	27.6
experiment	HF/6-31G*	69.4	34.7
experiment	HF/DZP	77.2	49.6
B3LYP/aug-cc-pVTZ	B3LYP/aug-cc-pVTZ (0)	25.2	7.6
B3LYP/aug-cc-pVDZ	B3LYP/aug-cc-pVDZ (0)	24.5	7.6
B3LYP/6-311++G(2d,2p)	B3LYP/6-311++G(2d,2p) (0)	24.1	7.6
experiment	B3LYP/aug-cc-pVTZ (0)	40.9	24.7
experiment	B3LYP/aug-cc-pVDZ (0)	34.6	21.9
experiment	B3LYP/6-311++G(2d,2p) (0)	34.2	20.9
HF/aug-cc-pVDZ	HF/aug-cc-pVDZ (0)	10.3	5.6
experiment	HF/aug-cc-pVDZ (0)	67.9	35.4
B3LYP/6-31G*	B3LYP/6-31G* (0)	19.9	7.0
B3LYP/DZP	B3LYP/DZP (0)	24.8	9.9
experiment	B3LYP/6-31G* (0)	49.1	27.5
experiment	B3LYP/DZP (0)	54.8	42.5
HF/6-31G*	HF/6-31G* (0)	9.5	5.3
HF/DZP	HF/DZP (0)	11.2	6.9
experiment	HF/6-31G* (0)	73.7	35.3
experiment	HF/DZP (0)	80.2	47.9
B3LYP/aug-cc-pVDZ	B3LYP/aug-cc-pVDZ (γ_s)[c]	42.1	27.0
experiment	B3LYP/aug-cc-pVDZ (γ_s)[c]	54.0	34.8

[a] $[\alpha]_D(0)$ and $[\alpha]_D$ are obtained using $\beta(0)$ and $\beta(D)$, respectively, where $\beta(0)$ and $\beta(D)$are calculated at the static limit, $\nu = 0$, and at the sodium D line frequency, respectively. The aug-cc-pVTZ basis set results are for 23 of the 30 molecules given in Figure 1 (excludes molecules #16, #19−23, and #26). All other basis set results include all 30 molecules. Experimental results are for 28 molecules (excludes #27 and #28). [b] Molecules #14 and #26 excluded. [c] $\gamma_s = (n^2_D + 2)/3$. Excludes molecules #27, #28, and #30.

1−**15**, **17**, **18**, **24**, **25**, and **27**−**30**. $[\alpha]_D$ values obtained for the three basis sets are compared in Figure 2. Average differences between calculations are given in Table 3. For all three basis set combinations, the mean absolute differences are <10°. The range of $[\alpha]_D$ values given by all three basis sets over 23 molecules varies from 2.5 to 29.6°. The range is >25° for molecules **3** (25.2°), **4** (29.6°) and **10** (28.4°). The aug-cc-pVTZ basis set is much larger than the aug-cc-pVDZ and 6-311++G(2d,2p) basis sets. In addition, the aug-cc-pVDZ and 6-311++G(2d,2p) basis sets are of quite different provenance. The consistently small variation among $[\alpha]_D$ values predicted using the three basis sets supports the conclusion that all three basis sets provide β(D) values close to complete basis set limiting values.

Comparison to experimental $[\alpha]_D$ values for the 28 molecules **1**−**26**, **29**, and **30** is shown in Figure 3. Average deviations between calculated and experimental $[\alpha]_D$ values are given in Table 3. For all three basis sets the mean absolute deviations are in the range 20−25°. The largest deviations are for molecules **6**, **13**, **14**, **26**, and **30**. The ranges of deviations for these molecules are **6**: 54.2−69.1; **13**: 36.3−56.7; **14**: 49.4−70.0; **26**: 32.8−54.5; and **30**: 48.9−52.8. As discussed in more detail below, the differences between calculated and experimental $[\alpha]_D$ values can be attributed to: (1) errors in β(D); (2) vibrational effects; (3) solvent effects; and (4) errors in experimental $[\alpha]_D$ values.

We have also carried out HF/SCF calculations at the aug-cc-pVDZ basis set level. β(D) and $[\alpha]_D$ values obtained for **1**−**30** are given in Table 2. HF/SCF and B3LYP aug-cc-pVDZ $[\alpha]_D$ values are compared in Figure 4. HF/SCF $[\alpha]_D$ values are compared to experiment in Figure 5. Average differences of HF/SCF and B3LYP $[\alpha]_D$ values and average deviations of HF/SCF and experimental $[\alpha]_D$ values are given in Table 3. HF/SCF and B3LYP $[\alpha]_D$ values differ on average by 55.4°. HF/SCF $[\alpha]_D$ values deviate from experiment on average by 62.7°. Very large differences between HF/SCF and B3LYP $[\alpha]_D$ values are exhibited by **14** and **26**: 609° and 347°, respectively. In both cases, HF/SCF $[\alpha]_D$ values are much further from the experimental values: deviations are 539° and 292° for **14** and **26**, respectively. If **14** and **26** are excluded, the average

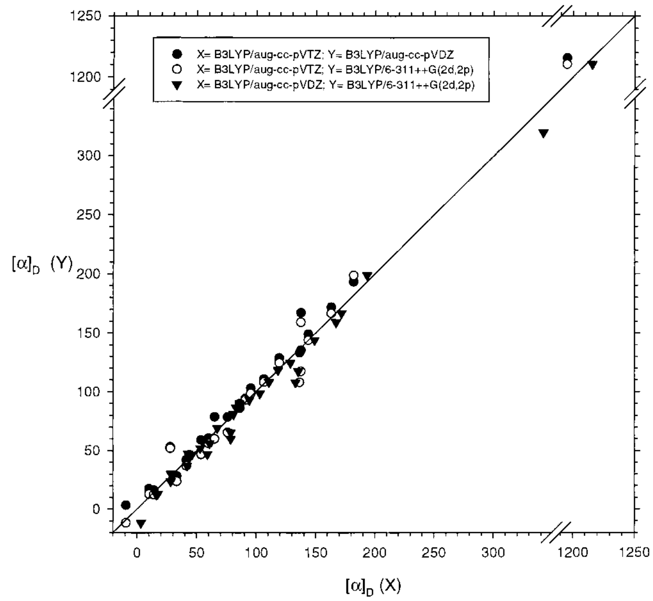

Figure 2. Comparison of $[\alpha]_D$ values obtained using B3LYP and the aug-cc-pVTZ, aug-cc-pVDZ and 6-311++G(2d,2p) basis sets. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

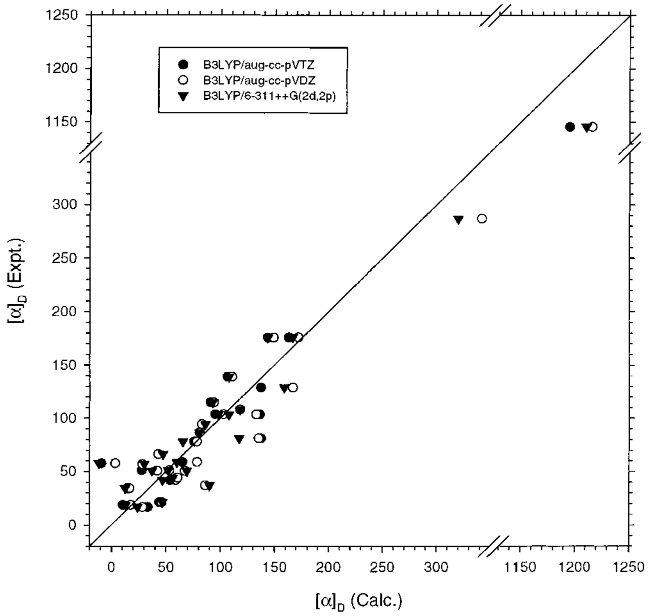

Figure 3. Comparison of $[\alpha]_D$ values obtained using B3LYP and the aug-cc-pVTZ, aug-cc-pVDZ and 6-311++G(2d,2p) basis sets to experimental $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

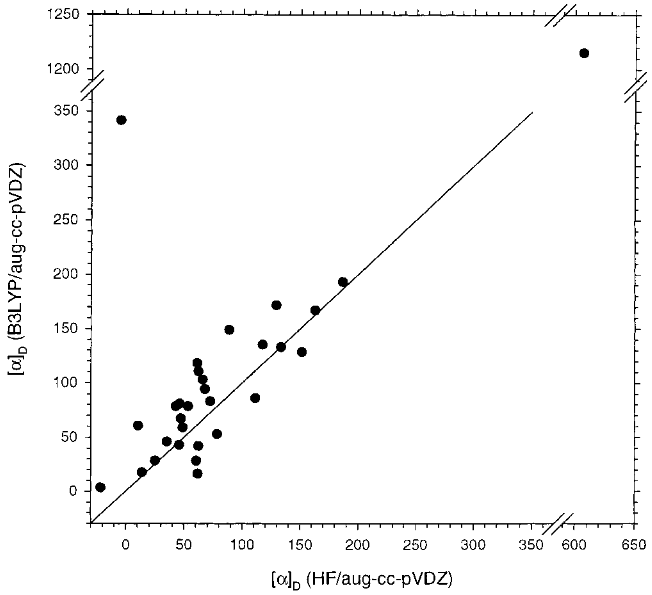

Figure 4. Comparison of B3LYP and HF/SCF $[\alpha]_D$ values obtained using the aug-cc-pVDZ basis set. The line has slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

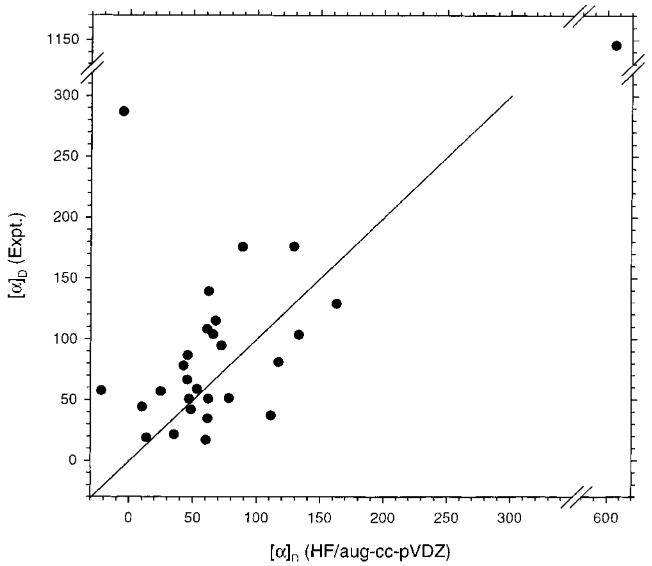

Figure 5. Comparison of HF/SCF $[\alpha]_D$ values obtained using the aug-cc-pVDZ basis set to experimental $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

difference of HF/SCF and B3LYP $[\alpha]_D$ values decreases to 25.2°, and the average deviation of HF/SCF $[\alpha]_D$ values from experiment decreases to 35.5°. B3LYP/aug-cc-pVDZ $[\alpha]_D$ values deviate from experiment on average by 23.1° when **14** and **26** are included and by 20.1° when **14** and **26** are ignored. The accuracy of the HF/SCF $[\alpha]_D$ values is thus substantially lower than the B3LYP values, whether or not **14** and **26** are included.

Values of β(D) and $[\alpha]_D$ obtained using the B3LYP functional and the two small basis sets 6-31G* and DZP are given in Table 4. $[\alpha]_D$ values are compared to B3LYP/aug-cc-pVDZ $[\alpha]_D$ values in Figure 6. Average differences between B3LYP 6-31G*, DZP, and large basis set $[\alpha]_D$ values are given in Table 3. B3LYP 6-31G* and DZP $[\alpha]_D$ values are compared to experiment in Figure 7. Average deviations are given in Table 3. The differences between 6-31G* and DZP $[\alpha]_D$ values range from 1.3 to 206.9°. The largest differences are for **3**:136.9°; **4**: 206.9°; **13**: 111.8°; **14**: 125.9°; and **26**: 170.9°. The average difference is 48.0°. The differences between 6 and 31G* and aug-cc-pVDZ $[\alpha]_D$ values range from 1.3 to 202.6°. The largest differences are for **4**: 64.8; **6**: 75.2°; **11**: 59.9°; **14**: 57.0°; **26**: 202.6°; and **27**: 54.6°. The average difference is 34.3°. The differences between DZP and aug-cc-pVDZ $[\alpha]_D$ values range from 0.6 to 142.1°. The largest differences are for **3**: 123.9; **4**: 142.1°; **13**: 104.0°; **14**: 57.0°; and **17**: 50.5°. The average difference is 33.2°. The average differences of B3LYP 6-31G* and DZP $[\alpha]_D$ values from B3LYP 6-311++G(2d,2p) and aug-cc-pVTZ values are also in the range 30−40°. The deviations between 6-31G* and experimental $[\alpha]_D$ values range from 0.9° to 148.1°. The largest deviations are for **6**: 129.4°; **11**: 65.1°; **14**: 112.9°; and **26**: 148.1°. The average deviation

TABLE 4: Small Basis Set Values of β and $[\alpha]_D$[a]

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	expt[c]	literature[d]
1	(2S)						−18.7	
		B3LYP/						
		6-31G*:	−0.0353	−0.0335	−23.52	−22.29		
		DZP:	0.0186	0.0229	12.37	15.23		
		HF/						
		6-31G*:	−0.0243	−0.0243	−16.17	−16.15		−18
		DZP:	0.0328	0.0367	21.84	24.42		
2	(2R,3R)						58.8	
		B3LYP/						
		6-31G*:	0.1524	0.1541	81.72	82.64		
		DZP:	0.0995	0.1025	53.39	54.98		
		HF/						
		6-31G*:	0.1082	0.1111	58.02	59.58		63[e]
		DZP:	0.0345	0.0342	18.48	18.35		
3	(2R)						51.2	
		B3LYP/						
		6-31G*:	0.0800	0.0769	41.73	40.11		
		DZP:	0.3061	0.3393	159.66	176.98		
		HF/						
		6-31G*:	0.1179	0.1289	61.50	67.26		55
		DZP:	0.2609	0.2876	136.11	150.04		
4	(2R,3R)						129.0	
		B3LYP/						
		6-31G*:	0.2330	0.2332	102.19	102.30		
		DZP:	0.6353	0.7049	278.68	309.20		
		HF/						
		6-31G*:	0.2758	0.3000	120.98	131.59		118
		DZP:	0.5386	0.5954	236.24	261.17		257
5	(1S,2S)						42	
		B3LYP/						
		6-31G*:	0.0655	0.0692	36.12	38.15		
		DZP:	0.0812	0.0944	44.77	52.04		
		HF/						
		6-31G*:	0.0562	0.0594	31.01	32.76		
		DZP:	0.0642	0.0721	35.39	39.76		41
6	(2R,3R)						57.6	
		B3LYP/						
		6-31G*:	−0.1087	−0.1525	−51.17	−71.80		
		DZP:	−0.0175	−0.0442	−8.25	−20.82		
		HF/						
		6-31G*:	−0.0627	−0.0850	−29.54	−40.03		
		DZP:	0.0250	0.0111	11.78	5.23		1
7	(2R,3R)						103.8	
		B3LYP/						
		6-31G*:	0.1347	0.1417	73.24	77.06		
		DZP:	0.1381	0.1495	75.08	81.31		
		HF/						
		6-31G*:	0.1069	0.1121	58.11	60.95		
		DZP:	0.0856	0.0910	46.56	49.47		54
8	(2R,3R)						−16.8	
		B3LYP/						
		6-31G*:	−0.0669	−0.0527	−24.50	−19.30		
		DZP:	−0.1592	−0.1625	−58.32	−59.54		
		HF/						
		6-31G*:	−0.1224	−0.1245	−44.85	−45.59		
		DZP:	−0.2089	−0.2203	−76.52	−80.69		−71
9	(1S,2R)						78.2	
		B3LYP/						
		6-31G*:	0.1306	0.1609	55.19	67.95		
		DZP:	0.0759	0.0962	32.09	40.63		
		HF/						
		6-31G*:	0.0719	0.0850	30.37	35.91		
		DZP:	0.0156	0.0224	6.60	9.45		−2
10	(1R,2R)						−103.4	
		B3LYP/						
		6-31G*:	−0.2359	−0.2500	−99.64	−105.63		
		DZP:	−0.3177	−0.3452	−134.23	−145.83		
		HF/						
		6-31G*:	−0.2289	−0.2444	−96.69	−103.25		
		DZP:	−0.2914	−0.3135	−123.11	−132.46		−113

TABLE 4: (Continued)

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	expt[c]	literature[d]
11	(3S)						≤−175.6	
		B3LYP/						
		6-31G*:	−0.1797	−0.1953	−101.99	−110.88		
		DZP:	−0.2783	−0.3177	−158.01	−180.39		
		HF/						
		6-31G*:	−0.1504	−0.1614	−85.41	−91.63		
		DZP:	−0.2290	−0.2555	−130.02	−145.06		−149
12	(4R)						−21.2	
		B3LYP/						
		6-31G*:	−0.0464	−0.0399	−15.19	−13.05		
		DZP:	−0.1242	−0.1387	−40.65	−45.41		
		HF/						
		6-31G*:	−0.0256	−0.0219	−8.39	−7.16		
		DZP:	−0.0901	−0.0989	−29.50	−32.38		−55
13	(S)						81.0	
		B3LYP/						
		6-31G*:	0.2075	0.2247	117.80	127.58		
		DZP:	0.3598	0.4216	204.29	239.38		
		HF/						
		6-31G*:	0.1824	0.1992	103.56	113.12		
		DZP:	0.2743	0.3141	155.70	178.30		176
14	(1S,4S)						−1146	
		B3LYP/						
		6-31G*:	−1.9507	−2.8883	−697.62	−1032.92		
		DZP:	−2.1849	−3.2403	−781.36	−1158.77		
		HF/						
		6-31G*:	−1.1828	−1.5226	−423.00	−544.50		
		DZP:	−1.3110	−1.6930	−468.85	−605.43		
15	(1R,4R)						44.1	
		B3LYP/						
		6-31G*:	0.0238	0.0934	6.06	23.72		
		DZP:	0.0957	0.1626	24.32	41.30		
		HF/						
		6-31G*:	−0.0421	−0.0299	−10.69	−7.61		
		DZP:	−0.0020	0.0054	−0.52	1.38		
16	(1R,4R)						−50.5	
		B3LYP/						
		6-31G*:	−0.2925	−0.3337	−74.31	−84.78		
		DZP:	−0.2149	−0.2619	−54.58	−66.54		
		HF/						
		6-31G*:	−0.2336	−0.2633	−59.35	−66.90		
		DZP:	−0.1788	−0.2098	−45.43	−53.29		
17	(1R)						51.6	
		B3LYP/						
		6-31G*:	0.2346	0.2659	66.60	75.49		
		DZP:	0.2775	0.3258	78.78	92.47		
		HF/						
		6-31G*:	0.2433	0.2737	69.08	77.69		
		DZP:	0.2671	0.3064	75.81	86.97		
18	(1R,5S)						115.0	
		B3LYP/						
		6-31G*:	0.2277	0.2428	77.15	82.25		
		DZP:	0.2175	0.2366	73.68	80.16		
		HF/						
		6-31G*:	0.1794	0.1902	60.78	64.45		
		DZP:	0.1589	0.1692	53.82	57.32		
19	(1R,5S,7S)						108.1	
		B3LYP/						
		6-31G*:	0.3056	0.3373	92.21	101.78		
		DZP:	0.2492	0.2750	75.20	82.99		
		HF/						
		6-31G*:	0.1977	0.2111	59.65	63.69		
		DZP:	0.1746	0.1864	52.70	56.24		
20	(1R,5S,7R)						94.4	
		B3LYP/						
		6-31G*:	0.2453	0.2512	74.01	75.79		
		DZP:	0.2974	0.3206	89.73	96.73		
		HF/						
		6-31G*:	0.2118	0.2204	63.92	66.50		
		DZP:	0.2100	0.2226	63.36	67.17		

TABLE 4: (Continued)

molecule #[b]	AC[b]	method	$\beta(0)$	$\beta(D)$	$[\alpha]_D(0)$	$[\alpha]_D$	expt[c]	literature[d]
21	(1R,5S,7S)						86.5	
		B3LYP/						
		6-31G*:	0.2892	0.3214	78.66	87.40		
		DZP:	0.2073	0.2275	56.39	61.88		
		HF/						
		6-31G*:	0.1877	0.2015	51.06	54.81		
		DZP:	0.1554	0.1661	42.28	45.17		
22	(1R,5S,7R)						66.3	
		B3LYP/						
		6-31G*:	0.1827	0.1865	49.68	50.71		
		DZP:	0.1693	0.1816	46.04	49.39		
		HF/						
		6-31G*:	0.1425	0.1517	38.74	41.25		
		DZP:	0.1679	0.1755	45.66	47.72		
23	(1R,5S)						56.9	
		B3LYP/						
		6-31G*:	0.1446	0.1575	39.33	42.83		
		DZP:	0.0978	0.1089	26.60	29.61		
		HF/						
		6-31G*:	0.1098	0.1175	29.87	31.95		
		DZP:	0.0885	0.0952	24.07	25.88		
24	(1S,5R)						175.8	
		B3LYP/						
		6-31G*:	0.3473	0.3855	115.67	128.39		
		DZP:	0.2780	0.3091	92.60	102.94		
		HF/						
		6-31G*:	0.2074	0.2251	69.08	74.96		
		DZP:	0.1729	0.1864	57.58	62.07		
25	(1S,5R)						139.2	
		B3LYP/						
		6-31G*:	0.3300	0.3686	98.05	109.53		
		DZP:	0.2183	0.2444	64.87	72.62		
		HF/						
		6-31G*:	0.1892	0.2068	56.22	61.45		
		DZP:	0.1448	0.1567	43.03	46.56		
26	(5R,11R)						−287	
		B3LYP/						
		6-31G*:	−0.4793	−0.8993	−74.05	−138.92		
		DZP:	−1.4323	−2.0056	−221.27	−309.83		
		HF/						
		6-31G*:	0.8728	0.9739	134.83	150.44		
		DZP:	0.2457	0.2852	37.96	44.07		
27	(2S)							
		B3LYP/						
		6-31G*:	−0.2599	−0.2798	−170.17	−183.18		
		DZP:	−0.1411	−0.1500	−92.39	−98.18		
		HF/						
		6-31G*:	−0.2559	−0.2761	−167.52	−180.77		
		DZP:	−0.1878	−0.2043	−122.95	−133.77		
28	(2R,3R)							
		B3LYP/						
		6-31G*:	0.3900	0.4142	206.37	219.13		
		DZP:	0.2942	0.3152	155.65	166.75		
		HF/						
		6-31G*:	0.3572	0.3810	189.00	201.60		
		DZP:	0.2923	0.3153	154.63	166.81		
29	(2S)						−34.5	
		B3LYP/						
		6-31G*:	−0.0071	−0.0098	−2.71	−3.73		
		DZP:	0.0050	0.0052	1.92	1.99		
		HF/						
		6-31G*:	−0.0679	−0.0796	−25.96	−30.42		
		DZP:	−0.0735	−0.0850	−28.11	−32.48		
30	(2S,3S)						−37.1	
		B3LYP/						
		6-31G*:	−0.1914	−0.2018	−64.25	−67.76		
		DZP:	−0.1963	−0.2088	−65.90	−70.11		
		HF/						
		6-31G*:	−0.2337	−0.2530	−78.48	−84.95		
		DZP:	−0.2324	−0.2526	−78.02	−84.81		

[a] Values of β are in atomic units; values of $[\alpha]_D$ assume $\gamma_s = 1$ (see text) and are in deg[dm·(gm/cc)]$^{-1}$. $\beta(0)$ and $\beta(D)$ are calculated at the static limit, $\nu = 0$, and at the sodium D line frequency respectively. $[\alpha]_D(0)$ and $[\alpha]_D$ are obtained using $\beta(0)$ and β(D) respectively. [b] See Figure 1.[c] From Table 1. [d] Prior HF calculations using GIAOs taken from Polavarapu, P.L. and Zhao, C. *Chem. Phys. Lett* **1998**, *296*, 105 with the $\gamma_s = (n_D^2 + 2)/3$ factor removed. [e] Results for 6-31G**.

is 33.1°. The deviations between DZP and experimental $[\alpha]_D$ values range from 2.3° to 158.4°. The largest deviations are for **3**: 125.8°; **4**: 180.2°; **6**: 98.4°; **13**: 158.4°; **24**: 72.9° and **25**: 66.6°. The average deviation is 42.9°.

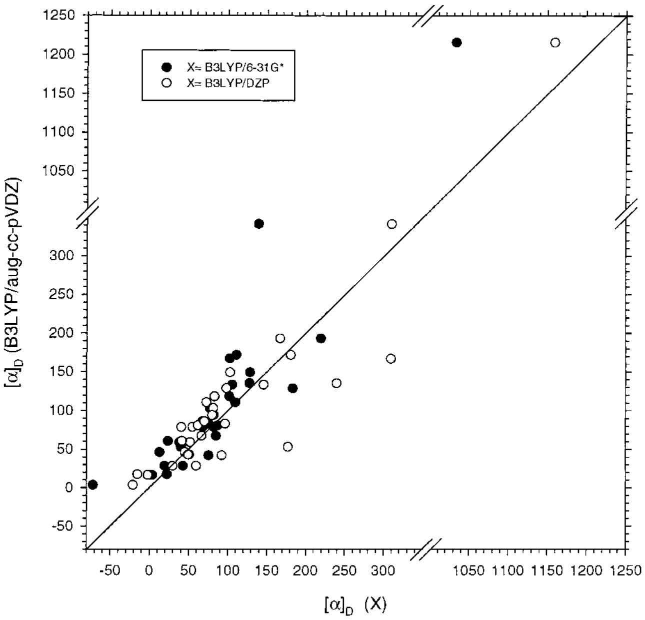

Figure 6. Comparison of $[\alpha]_D$ values obtained using B3LYP and the 6-31G* and DZP basis sets to B3LYP/aug-cc-pVDZ $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

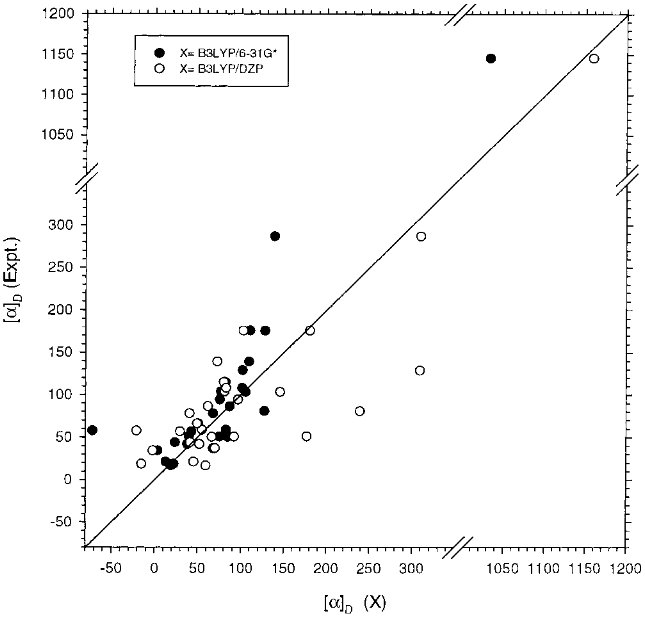

Figure 7. Comparison of $[\alpha]_D$ values obtained using B3LYP and the 6-31G* and DZP basis sets to experimental $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

The variation in $[\alpha]_D$ values between the 6-31G* and DZP basis sets is much larger than for the aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p) basis sets. The differences in 6-31G* and DZP $[\alpha]_D$ values from the aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p) values are much larger than the differences in $[\alpha]_D$ values given by the three large basis sets. 6-31G* and DZP $[\alpha]_D$ values are in substantially worse agreement with experiment than are the large basis set $[\alpha]_D$ values. Clearly, the small basis sets yield $[\alpha]_D$ values of lower accuracy than the large basis sets.

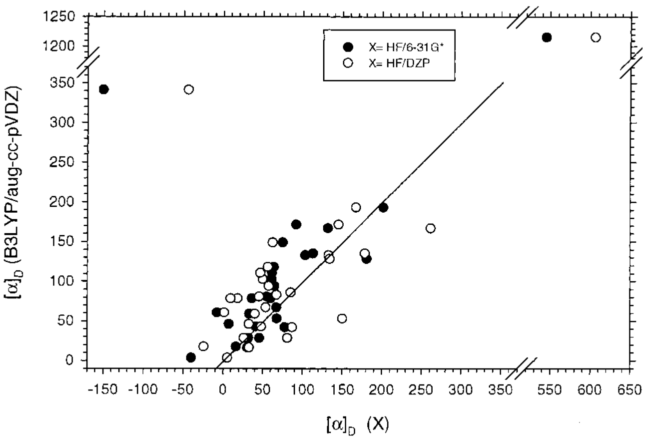

Figure 8. Comparison of HF/SCF $[\alpha]_D$ values obtained using the 6-31G* and DZP basis sets to B3LYP/aug-cc-pVDZ $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

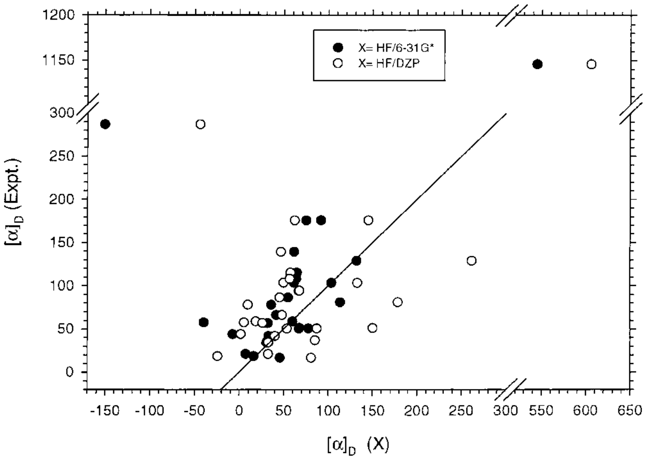

Figure 9. Comparison of HF/SCF $[\alpha]_D$ values obtained using the 6-31G* and DZP basis sets to experimental $[\alpha]_D$ values. The line is of slope +1. Absolute configurations are those for which experimental $[\alpha]_D$ values are positive.

6-31G* and DZP calculations of β(D) and $[\alpha]_D$ have also been carried out at the HF/SCF level. The results are given in Table 4. $[\alpha]_D$ values are compared to B3LYP/aug-cc-pVDZ values in Figure 8. Average differences between HF/SCF 6-31G* and DZP $[\alpha]_D$ values and B3LYP and HF/SCF aug-cc-pVDZ $[\alpha]_D$ values are given in Table 3. $[\alpha]_D$ values are compared to experiment in Figure 9. Average deviations are given in Table 3. Average differences of HF 6-31G* and DZP $[\alpha]_D$ values from B3LYP large basis set values lie in the range 55−70°. Average differences from B3LYP 6-31G* and DZP values are 45.1° and 52.8° respectively. Average differences from HF aug-cc-pVDZ values are 20.7° and 22.3° for 6-31G* and DZP, respectively. Average deviations from experiment for 6-31G* and DZP $[\alpha]_D$ values are 69.4° and 77.2°, respectively. These deviations can be compared to those for B3LYP 6-31G* and DZP $[\alpha]_D$ values, 33.1° and 42.9°, and to that for HF/ aug-cc-pVDZ values, 62.7°. Relative to B3LYP calculations at the same basis set level, and to HF/SCF calculations at a large basis set level, HF/SCF 6-31G* and DZP calculations are less accurate. As for HF/SCF aug-cc-pVDZ $[\alpha]_D$ values, molecules **14** and **26** contribute disproportionately to the differences between HF/SCF and B3LYP results and to the deviations of HF/SCF $[\alpha]_D$ values from experiment. Average differences between HF/SCF 6-31G* and DZP $[\alpha]_D$ values and B3LYP values and average deviations of HF/SCF 6-31G* and DZP $[\alpha]_D$ values from experimental values are substantially reduced when **14** and **26** are omitted (Table 3).

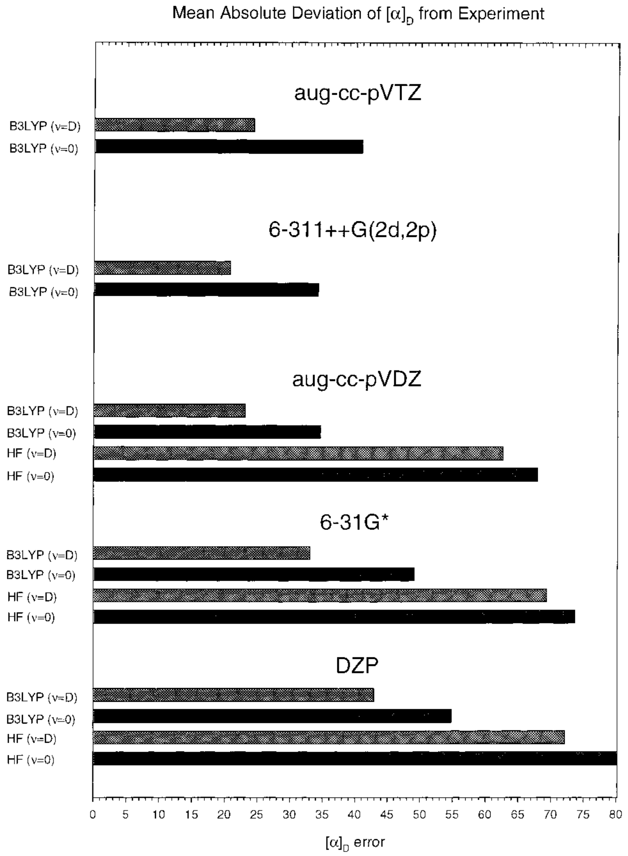

Figure 10. Mean absolute deviations of calculated and experimental $[\alpha]_D$ values.

The accuracies of B3LYP calculations using the 6-31G*, DZP, 6-311++G(2d,2p), aug-cc-pVDZ, and aug-cc-pVTZ basis sets and HF/SCF calculations using the 6-31G*, DZP, and aug-cc-pVDZ basis sets are summarized in Figure 10. It is clear that

(1) B3LYP calculations are more accurate than HF/SCF calculations;

(2) 6-311++G(2d,2p), aug-cc-pVDZ, and aug-cc-pVTZ calculations are more accurate than 6-31G* and DZP calculations.

In all calculations discussed so far, β has been calculated at the sodium D line frequency. To evaluate the relative accuracy of $[\alpha]_D$ values obtained using static limit β values, we have calculated $\beta(0)$ simultaneously with $\beta(D)$. Values of $\beta(0)$ and $[\alpha]_D$ derived thence, $[\alpha]_D(0)$, are given in Tables 2 and 4. Statistics obtained using these results are given in Table 3. We examine first $[\alpha]_D(0)$ values obtained using B3LYP and the three large basis sets (Table 2). $[\alpha]_D(0)$ and $[\alpha]_D$ values are compared in Figure 11. Average differences are given in Table 3. For all three basis sets, the mean absolute differences are 24−26°. For the majority of molecules, $\beta(0)$ and $\beta(D)$ values, and hence $[\alpha]_D$ values do not differ greatly. For molecules **14** and **26**, however, the differences in $[\alpha]_D$ are very large: ~400° for **14** and ~100° for **26**. When omitted, the mean absolute differences for the three basis sets decrease to 7.6°.

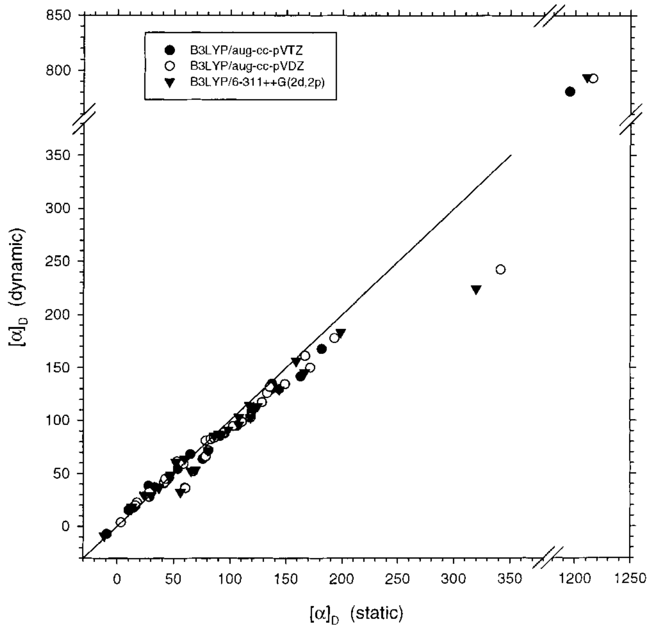

Figure 11. Comparison of $[\alpha]_D$ values calculated using static and dynamic β values ($\beta(0)$ and $\beta(D)$). The functional is B3LYP. The basis sets are aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p).

In examining the variation of β with frequency it is instructive to examine not only the absolute variation but also the percentage variation. For the majority of molecules, the percentage variation in β lies in the range from −25% to +25% for all three basis sets. For four molecules, **14**−**16** and **26**, the variation lies considerably outside this range. For example, the percentage variations at the aug-cc-pVDZ basis set level are: **14**: 53.3; **15**: 68.7; **16**: 30.2; and **26**: 41.0. We attribute these larger variations to the presence of specific chromophoric groups: the C═O group in **14**−**16** and the phenyl groups in **26**. In the case of **15** and **16**, the absolute values of $[\alpha]_D$ are < 100° and large percentage variations give relatively small absolute variations. However, in the cases of **14** and **26**, the absolute values of $[\alpha]_D$ are much larger, over 1000° in **14**, and large percentage variations yield much larger absolute variations.

It is also interesting to note that for some molecules, β decreases in absolute magnitude from $\beta(0)$ to $\beta(D)$. From eq 6, it is natural to expect that $\beta(\nu)$ will increase with increasing frequency and, therefore, that $\beta(D) > \beta(0)$ and $[\alpha]_D > [\alpha]_D(0)$. For the majority of molecules, this is the case. However, for **1**, **2**, **3**, **6**, **8**, **22** and **29**, the opposite is the case.

Average deviations of B3LYP large basis set values of $[\alpha]_D(0)$ from experiment (Table 3) are substantially larger than for $[\alpha]_D$: 34.2−40.9° compared to 20.8−24.3°. Without molecules **14** and **26** the deviations for $[\alpha]_D(0)$ are lowered to 20.9−24.7° compared to 18.7−23.0 for $[\alpha]_D$ (Table 3). Thus, when **14** and **26** are not included the average deviations of $[\alpha]_D(0)$ and $[\alpha]_D$ from experiment are very similar.

Differences between $[\alpha]_D(0)$ and $[\alpha]_D$ values calculated at the B3LYP 6-31G* and DZP levels and at the HF/SCF 6-31G*, DZP and large basis set levels (Table 3) parallel those at B3LYP/large basis set levels.

All calculated $[\alpha]_D$ values discussed above have been obtained assuming $\gamma_s = 1$ i.e., solvent effects on $[\alpha]_D$ have been neglected. The expression $\gamma_s = (n^2 + 2)/3$, based on a simple continuum dielectric solvent model,[2b] is often used to account for solvent effects on optical rotations. Values of $[\alpha]_D$ obtained using B3LYP/ aug-cc-pVDZ values of $\beta(D)$ and $\gamma_s = (n_D^2 + 2)/3$ are given in Table 2. The average difference between solvent-uncorrected and -corrected $[\alpha]_D$ values is 42.8°. The average deviation of solvent-corrected $[\alpha]_D$ values from experimental $[\alpha]_D$ values is 54.7°. Thus, inclusion of the factor $\gamma_s = (n_D^2 + 2)/3$ leads to substantial deterioration of the agreement with experiment.

Discussion

Two results are of primary importance. First, the B3LYP calculations using the 6-311++G(2d,2p), aug-cc-pVDZ and aug-cc-pVTZ basis sets yield very similar $[\alpha]_D$ values. The maximum range for all three basis sets is <30°; the average differences between pairs of basis sets are <10°. Since 6-311++G(2d,2p) and aug-cc-pVDZ are quite different basis sets and since aug-cc-pVTZ is approximately twice as large as either, this consistency confirms the conclusion of our prior study[12] that all three basis sets provide good approximations to complete basis set rotations. Second, the large basis set B3LYP calculations yield $[\alpha]_D$ values whose mean absolute deviations from experimental $[\alpha]_D$ values are in the range 20−25°. Although for the majority of molecules the deviations are <40° for all three basis sets, for a few molecules − **6**, **13**, **14**, **26**, and **30**, significantly larger deviations occur. For two molecules, **14** and **26**, the absolute magnitudes of $[\alpha]_D$ are large (in **14**, over 1000°) and on a percentage basis the deviations are not exceptional. In contrast, for molecules **6**, **13**, and **30**, the absolute magnitudes of $[\alpha]_D$ are <100° and on a percentage basis the deviations remain exceptionally large.

A number of factors could contribute to the deviations of calculated values from experiment. **First: imperfection in the B3LYP functional**. B3LYP is not an exact functional for frequency-independent properties, and in addition, we have used the adiabatic approximation[14d] for the exchange-correlation functional in calculating the frequency dependence of $\beta_{\alpha\beta}$. It is difficult to predict the magnitude of the errors arising from the choice of the B3LYP functional and the use of the adiabatic approximation. We note that a limited set of calculations for **1**, **4**, and **18**[12,13] using four hybrid functionals have yielded small variations in rotation, showing that for this limited range of functionals the sensitivity to the choice of functional is small. **Second: basis set error**. From the discussion above, we conclude that, on average, basis set error should be <10°. It is likely that, although significant, it is not the dominant contributor. **Third: equilibrium geometry errors**. The B3LYP/6-31G* geometries we have used are of well-documented accuracy.[11a] It is possible that the use of more accurate geometries would yield significantly more accurate rotations. A limited set of calculations for **1**, **4**, and **18**,[12,13] using a variety of geometry choices, have found some sensitivity to this parameter, suggesting that errors in B3LYP/6-31G* geometries may indeed contribute significantly to deviations of calculated rotations. Further studies are required to quantitate this contribution on a statistical basis. **Fourth: vibrational effects**. Our calculations neglect vibrational effects (the factor γ_v in eqs 7 and 8). For other polarizabilities, vibrational effects have been shown to contribute significantly,[21] and this is likely to be the case for $\beta_{\alpha\beta}$. Further studies are required to evaluate these contributions. **Fifth: solvent effects**. In our comparison to experimental $[\alpha]_D$ values, we have ignored solvent effects (the factor γ_s in eqs 4 and 8). These can be substantial.[22] For example, a thorough examination of the solvent dependence of $[\alpha]_D$ for **1** over a range of 35 solvents found a variation of 34.9°.[23] Variations of this magnitude are quite common. It is very likely, therefore, that the neglect of solvent effects in our calculations is a major contributor to the deviations from experiment. The factor γ_s has been traditionally approximated by $\gamma_s = (n^2 + 2)/3$.[2b] However, we have shown that use of this expression for γ_s, together with B3LYP/aug-cc-pVDZ calculations leads to a significant *lowering* of the agreement of calculated and experimental $[\alpha]_D$ values. Thus, a more sophisticated treatment of γ_s is necessary. At this time, we are implementing and evaluating the application of the Polarizable Continuum Model (PCM) methodology[24] to the prediction of solvent effects on optical rotations. Preliminary calculations for the molecules **18**−**23** have yielded some improvement in calculated rotations.[13] Further studies for a wider range of molecules are under way. **Sixth: experimental error**. The accuracies of the experimental values of $[\alpha]_D$ for the 28 molecules studied here are not very well-defined and are likely to vary considerably. For some of the molecules experimental error should be much less than calculational error. For others, experimental error could be comparable to calculational error. The two largest sources of error in experimental $[\alpha]_D$ values are likely to arise from uncertainties in ee and from concentration effects. For some of the 28 molecules studied here, ee's were measured; however, both the magnitude and the accuracy of measured ee's vary widely. For other molecules, ee's were not measured. Rotations are generally measured at quite high concentrations (>0.01 M), in some cases in neat liquids, and concentration dependence has rarely been determined. In some cases, the experimental values may be significantly affected by intermolecular interactions. Further studies of molecules whose ee's are precisely known and whose rotations are measured as a function of concentration, in order to obtain dilute solution $[\alpha]_D$ values, will be necessary to provide optimal comparison of experimental data to theory.

For the aug-cc-pVDZ basis set we have carried out calculations at the HF/SCF level for comparison to the B3LYP/aug-cc-pVDZ calculations. At this basis set level, the average difference of HF/SCF and B3LYP $[\alpha]_D$ values for 30 molecules is 55.4°. The mean absolute deviation of HF/SCF $[\alpha]_D$ values from experiment for 28 molecules is 62.7°, compared to 23.1° for B3LYP. Two molecules, **14** and **26**, exhibit exceptionally large differences between HF/SCF and B3LYP rotations. When they are excluded, the average difference between HF/SCF and B3LYP $[\alpha]_D$ values drops to 25.2°, and the average deviation of HF/SCF $[\alpha]_D$ values from experiment drops to 35.5°. The average deviation of B3LYP $[\alpha]_D$ values from experiment changes to 20.1°, a small decrease. Whether or not **14** and **26** are included, our results demonstrate that B3LYP $[\alpha]_D$ values are substantially more accurate than HF/SCF values. This finding is to be expected. Across a broad range of molecular properties, DFT/B3LYP calculations have been shown to provide results systematically superior to HF/SCF results.[11] The exceptionally large differences between HF/SCF and B3LYP $[\alpha]_D$ values for **14** and **26** are somewhat surprising since the electronic and geometrical structures of these molecules are not unusual. However, the fact that they are not unusual molecules leads to the expectation that similarly large differences will be regularly observed in future studies, eventually rendering the results for **14** and **26** unexceptional.

Rotations calculated using B3LYP together with the 6-31G* and DZP basis sets have been compared to the large basis set B3LYP values and to experiment. 6-31G* and DZP rotations differ, on average, by 48.0°. The largest difference is 206.9°. The average and maximum differences are much larger than those obtained comparing pairs of large basis sets. 6-31G* and DZP $[\alpha]_D$ values differ from large basis set values on average by 30−40°, and from experimental values by 33.1° and 42.9° respectively. These results show that the small basis set rotations are substantially less accurate than the large basis set rotations and that the two small basis sets do not give consistent predictions. Our results are fully consistent with those reported previously for **1** and **4** for a much larger range of basis sets.[12] The prior study showed that calculated rotations exhibit slow basis set convergence and that small basis sets generally gave results in poor agreement with large basis set results. Variation of calculated rotations with basis set size was not monotonic and small basis sets of similar size gave very variable rotations. The 6-31G* basis set gives a somewhat lower average deviation between calculated and experimental $[\alpha]_D$ values (33.1°) than the DZP basis set (42.9°). The difference between the basis sets is accentuated when molecules **14** and **26** are excluded, the deviations then decreasing to 25.6° for 6-31G* and increasing to 44.8° for DZP. The apparently greater accuracy of 6-31G* over DZP is surprising because the latter is larger (including polarization functions on H atoms) and generally superior to 6-31G* in accuracy. The difference between 6-31G* and DZP diminishes when $[\alpha]_D$ values are compared to large basis set values.

Given the B3LYP/6-31G* and /DZP results and the HF/SCF/aug-cc-pVDZ results, it is not surprising that HF/SCF calculations using the 6-31G* and DZP basis sets are both less accurate than HF/SCF aug-cc-pVDZ calculations and less accurate than B3LYP 6-31G* and DZP calculations.

Optical rotation calculations have been previously reported for many of the molecules **1**−**30**. Polavarapu[7a] reported calculations of $[\alpha]_D$ for **1**−**4** using the Amos methodology in CADPAC. Basis sets/geometries (all HF/SCF) were **1**: 6-31G/6-31G, 6-31G*/6-31G*, 6-31G(ext)/6-31G*; **2**: 6-31G**/6-31G**, 6-31G(ext)/6-31G**; **3**: 6-31G*/6-31G*, 6-31G(ext)/6-31G*; and **4**: 6-31G*/6-31G*, DZP/6-31G*. Polavarapu and Chakraborty[7c] reported calculations of $[\alpha]_D$ for **5**−**13**, again using CADPAC. Basis sets were 6-31G* and DZP; geometries were HF/SCF/6-31G*. Polavarapu and Zhao[7d] reported calculations of $[\alpha]_D$ for **1**−**13** carried out using the Helgaker et al. methodology in DALTON. β(D) values obtained using both FIAOs and GIAOs were used to calculate $[\alpha]_D$. Basis sets/geometries (all HF/SCF) were **1**, **3**: 6-31G*/6-31G*; **2**: 6-31G**/6-31G**; **4**: 6-31G*/6-31G* and DZP/6-31G*; and **5**−**13**: DZP/6-31G*. Polavarapu and Chakraborty[7e] reported calculations of $[\alpha]_D$ for **27** and **28**, using CADPAC. Basis sets were 6-31G* and DZP; geometries were HF/SCF/6-31G*. Kondru et al.[8b] reported calculations of sodium D line molar rotations for **24** and **25** using CADPAC. Basis sets were 6-31G, 6-31G* and 4-31G*. Geometries were not specified.

As we have discussed above and previously,[12] CADPAC calculations and DALTON calculations using FIAOs yield origin-dependent rotations. Their comparison to experiment is not meaningful. We make no attempt here to discuss the results reported using these methods. $[\alpha]_D$ values obtained using DALTON, GIAOs, and the 6-31G* and DZP basis sets are listed in Table 4. They are close to our HF/SCF 6-31G* and DZP results. The differences are attributable to differences in geometry and (possibly), in the case of DZP calculations, to differences in basis set. [The DZP basis set used by Polavarapu and co-workers was taken from the CADPAC basis set library;[9] there are several DZP basis sets in this library, and it is not clear which was used.]

With the exception of molecule **6**, all B3LYP large basis set calculations give $[\alpha]_D$ values of the same sign as observed $[\alpha]_D$ values. Our calculations therefore support the literature ACs. In the case of **6**, B3LYP aug-cc-pVTZ and 6-311++G(2d,2p) calculations give small, negative $[\alpha]_D$ values for R,R-**6**, while the B3LYP aug-cc-pVDZ $[\alpha]_D$ is small and positive. All three $[\alpha]_D$ values differ from the experimental $[\alpha]_D$ value by substantially more than the average deviation. Clearly, our results neither confirm nor contradict the literature AC of **6**.

Molecules **27** and **28** were included in this work since Polaravapu and Chakravorty[7e] compared calculations on these molecules to experimental $[\alpha]_D$ values for molecules **29** and **30** respectively, assuming that *N*-methyl and *N*-*tert*-butyl oxaziridines would possess very similar rotations. Our calculations for **27**−**30** show that this assumption is erroneous.

Conclusion

We have evaluated the accuracy of a new methodology for calculating $\beta(\nu)$ and hence $[\alpha]$, using DFT and GIAOs. Calculations have used the B3LYP functional and a range of basis sets. In parallel, HF/SCF calculations, also using GIAOs, have been carried out. We have shown, using a large set of chiral organic molecules, that B3LYP $[\alpha]_D$ values are substantially more accurate than HF/SCF $[\alpha]_D$ values. We have also shown that for both DFT and HF/SCF calculations $[\alpha]_D$ values are strongly basis set dependent. The large basis sets, aug-cc-pVTZ, aug-cc-pVDZ, and 6-311++G(2d,2p), all containing diffuse functions, give very consistent results. The small basis sets 6-31G* and DZP give much less consistent results. We have obtained average deviations of calculated $[\alpha]_D$ values from experimental values. B3LYP calculations using the large basis sets give mean absolute deviations over 28 molecules of 20−25°. At the 6-31G* and DZP basis set levels, the deviations are 33.1° and 42.9° respectively. HF/SCF/aug-cc-pVDZ calculations give a deviation of 62.7°. HF/SCF 6-31G* and DZP calculations give deviations of 69.4° and 77.2°.

In principle, the absolute configuration (AC) of a chiral molecule can be established by comparison of the experimental $[\alpha]_D$ value to an ab initio prediction for a known AC. Utilization of this protocol requires that the accuracy of the ab initio methodology in predicting $[\alpha]_D$ is such that calculational error is much less than the experimental $[\alpha]_D$ value. Our results thus define the lower limits of experimental $[\alpha]_D$ values permitting the utilization of the DFT/GIAO and HF/SCF/GIAO methodologies at various basis set levels. B3LYP large basis set calculations are sufficiently accurate to permit the determination of AC for molecules whose experimental $[\alpha]_D$ is $\gg$ 20−25°. HF/SCF 6-31G* and DZP calculations are much less reliable and are only useful when experimental $[\alpha]_D$ values are well over 100°.

These conclusions apply to the calculation of $[\alpha]_D$ values of rigid molecules. In the case of conformationally flexible molecules, the experimental $[\alpha]_D$ value is a weighted average of the values for all thermally populated conformations (eq 2). Calculated $[\alpha]_D$ values are then less accurate for two reasons. First, the $[\alpha]_D$ values of different conformations will often differ in sign, reducing the magnitude of predicted $[\alpha]_D$ values. Second, errors due to uncertainties in conformational populations (α_c in eq 2) are introduced.

Kondru et al. have assigned the ACs of three molecules using $[\alpha]_D$ values calculated ab initio.[8c,8d,8e] One molecule, an indolinone,[8d] is conformationally rigid; two molecules, an indoline[8c] and pitiamide A,[8e] are conformationally flexible. In all three cases, experimental $[\alpha]_D$ values are small: 59°,[8c] 16°[8d] and 10°.[8e] Ab initio calculations of $[\alpha]_D$ were carried out at the HF/SCF level using small basis sets. The results of this paper show that the accuracies of the predicted $[\alpha]_D$ values are insufficient to permit reliable assignment of ACs for these molecules.

Since HF/SCF $[\alpha]_D$ values are less accurate than DFT $[\alpha]_D$ values at any basis set level, and since the computational demands of DFT calculations are only a little greater than those of HF/SCF calculations, there appears to be no practical reason to use the HF/SCF methodology in the future. By contrast, computational effort increases rapidly with increasing basis set size. Although for many molecules the use of the aug-cc-pVDZ and 6-311++G(2d,2p) basis sets (or larger) will be practicable, above a threshold molecular size, this is no longer the case. To be carried out at all, calculations then require a smaller basis set. Our work has defined the substantial reduction in accuracy associated with the use of the 6-31G* and DZP basis sets. It is likely that basis sets of intermediate size will provide a better compromise of accuracy and computational cost; further statistical studies are required to evaluate likely candidate basis sets.

Acknowledgment. NSF grant CHE-9902832 to P.J.S. is gratefully acknowledged.

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