Absolute Stereochemistry of Chiral Molecules from ab Initio Theoretical and Experimental Molecular Optical Rotations

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Abstract: Optical rotations of a diverse set of chiral molecules have been calculated ab initio. In a majority of the molecules considered, the signs of the calculated optical rotations are in agreement with those of the corresponding experimental observations, and the magnitudes are in reasonable agreement. It is thus suggested that the ab initio optical rotations provide a convenient alternative approach to determine the absolute stereochemistry of chiral molecules. A group of molecules has also been identified where the sign of optical rotation predicted for a given configuration is at variance with the literature assignments, and further investigations are needed.

Introduction

Optical activity[1,2] is one of the oldest research tools that is routinely practiced by chemists. Optical rotatory dispersion (optical rotation versus wavelength) and circular dichroism are the two components of this optical activity that can be used to elucidate the absolute stereochemistry of chiral molecules.[1,2] The measurement of optical rotation in the visible spectral region for liquid samples is routine, and it is an established practice for organic chemists to measure and report the optical rotation of any synthesized chiral substance. In principle, the sign and magnitude of observed optical rotation should contain the information about absolute stereochemistry of the molecule under consideration. Although the theory of optical rotation[3] is known for a long time, reliable pathways to achieve a transparent connection between the measured optical rotation and the absolute stereochemistry have not been well established in the past. A majority of the studies have emphasized the use of electronic circular dichroism (ECD)[4] instead because of the relative ease in the use of quantum theoretical methods for predicting the rotational strength of an electronic transition that is needed for calculating the ECD. For corresponding prediction of the optical rotation, the optical rotation equation in its standard form[3] requires a knowledge of the rotational strengths for transitions to all of the excited electronic states. This is relatively difficult because here one needs an accurate knowledge of all of the excited electronic states. This situation was evident in the statement of Eyring et al.:[3b] "Since the eigenfunctions of complex molecules are not known to any high degree of accuracy, it has not as yet proved possible to determine the absolute configuration of any molecule by actual calculation". Nevertheless, attempts have been made[5] in predicting the optical rotatory dispersion for specific systems with some approximations.

Despite the enormous advances made in recent years in the use and applications of ab initio quantum mechanical methods, general quantum mechanical methods for predicting the optical rotations were lacking. This is in clear contrast to the corresponding developments for predicting electronic circular dichroism.[4] In their absence, empirical and semiempirical methods[6] for optical rotation predictions have been advanced. Vibrational circular dichroism (VCD),[7] and vibrational Raman optical activity (VROA)[8] are alternate properties that are being currently used for determining the absolute stereochemistry of chiral molecules. Although much progress has been made in the quantum mechanical predictions of VCD[9] and VROA,[10] the experimental measurement of these properties is not as facile for a synthetic chemist as of the optical rotation has been. A routine practical approach to predict the optical rotations reliably

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from the first principles would therefore be greeted with excitement by many practicing chemists, because such an approach would complement the experimentally routine and facile measurement of optical rotation. A comparison of the observed optical rotations with reliable theoretical predictions would enable the determination of the absolute stereochemistry of chiral molecules.

Recently one of us reported an ab initio quantum mechanical procedure[11] for predicting molecular optical rotations and demonstrated[11,12] an encouraging agreement between the observed and predicted optical rotations. In order for this approach to be generally accepted it is necessary to investigate the general applicability of this procedure to a diverse set of chiral molecules of known stereochemistry and identify the limitations, if any. In this paper, we therefore extend this ab initio approach for optical rotations to a diverse set of chiral molecules and identify its strength and weakness. A better understanding of these issues will provide impetus for solving related stereochemical problems.[13]

Theoretical Methodology

The theoretical quantity pertinent here is the electric dipole−magnetic dipole polarizability tensor, given by the expression[14−16]

$$G'_{\alpha\beta} = \frac{-4\pi}{h}\sum_{n\neq s}\frac{\omega}{\omega_{ns}^2 - \omega^2} Im\{\langle\psi_s^0|\hat{\mu}_\alpha|\psi_n^0\rangle\langle\psi_n^0|\hat{\mathrm{m}}_\beta|\psi_s^0\rangle\} \quad (1)$$

where $\hat{\mu}_\alpha$ and $\hat{\mathrm{m}}_\beta$ are respectively, the electric dipole moment and magnetic dipole moment operators; ψ_s^0 and ψ_n^0 represent the ground and excited electronic state wave functions, respectively; $\omega_{\mathrm{ns}} = 2\pi(E_n^0 - E_s^0)/h$, where E_n^0 and E_s^0 are the unperturbed energies of states n and s, respectively; ω is the angular frequency of exciting radiation. It is useful to define the quantity

$$\beta = -\omega^{-1}(G'_{xx} + G'_{yy} + G'_{zz})/3 \quad (2)$$

which is related to the optical rotation ϕ (in radians/cm) as[3]

$$\phi = 4\pi N\beta\omega^2\,(n^2+2)/3c^2 \quad (3)$$

where N represents the number of molecules per unit volume, n represents the refractive index of the medium, and $\omega^{-1}\mathrm{G}'_{\alpha\alpha}$ are in CGS units. When $\omega^{-1}\mathrm{G}'_{\alpha\alpha}$ are expressed in SI units, the right-hand side of eq 3 is to be multiplied with $\mu_0 c^2/4\pi$. The experimental optical rotations are most commonly reported as specific rotation [α] in units of deg/[dm·(gm/cc)]. The corresponding theoretical quantity is $[\alpha] = 3600\ \phi\ V_{\mathrm{m}}/2\pi M$ where M and V_{m} are, respectively, the molar mass and molar volume. Using these definitions, a convenient expression for the specific rotation is given[11] as

$$[\alpha] = 0.1343 \times 10^{-3}\,\beta\bar{\nu}^2(n^2+2)/3M \quad (4)$$

with β in units of (bohr),[4] M in gm/mol and $\bar{\nu}$ (wavenumber at which the optical rotation is measured) in cm^{-1}.

Table 1. Ab Initio Theoretical and Experimental Optical Rotations for Different Classes of Molecules

molecule	confgrtn	optical rotation,$[\alpha]_D$ calcd 631G*	calcd DZP	expt
trans-1,2-dimethylcyclopropane	(1*S*,2*S*)	+9.94	+82.1	+42[a]
trans-2,3-dimethyl-1-methylenecyclopropane	(2*R*,3*R*)	−64.3	+31.0	+57.6[b]
trans-1,2-difluorocyclopropane	(1*S*,2*S*)	−19.6	+9.29	?
trans-1,2-dichlorocyclopropane	(1*S*,2*S*)	+66.0	+91.6	?
2-methyloxetane	(2*S*)	+26.4	+29.4	+33.5[c]
2-methylthiitane	(2*S*)	−83.4	−148	−133[d]
2-methylthietane-1,1-dioxide	(2*S*)	−8.37	−29.4	−21.0[e]
4-methylthiete-1,1-dioxide	(4*R*)	−41.3	−76.8	−21.2[f]
3-methylcyclobutene	(3*S*)	−95.7	−176	−176[g]
1,3-dimethylallene	(a*S*)	+108	+207	+227[h]
trans-2,3-dimethylaziridine	(2*R*,3*R*)	+44.6	+46.2	+103.8[i]
N-chloro-*trans*-2,3-dimethylaziridine	(2*R*,3*R*)	−42.6	−97.0	−16.8[j]

[a] The experimental $[\alpha]_D$ reported for 0.5 M solution of (*R*,*R*)-(−)-enantiomer in pentane is multiplied by −1; see ref 22; refractive index is assumed to be ~1. [b] Experimental $[\alpha]_D$ reported for 1.72 M solution of (2S,3S)-(−)-enantiomer in CCl_4 is multiplied by −1; see ref 23; refractive index is assumed to be ~1. [c] Reference 25. [d] Value reported here is for 2.5 M solution of (2*S*)-(−)-propylthiitane in $CHCl_3$: see ref 26; refractive index is assumed to be ~1. [e] $[\alpha]_D$ value reported for 9.7 M solution of (2*R*)-(+)-enantiomer in C_2H_5OH is multiplied by −1; see ref 27. [f] $[\alpha]_D$ value reported for 5.99 M solution of (−)-enantiomer in $CHCl_3$; see ref 27. [g] $[\alpha]_D$ value reported for (+)-enantiomer (neat) with 66% optical purity is scaled to 100% and multiplied by −1; see ref 28. [h] See ref 29. [i] $[\alpha]_D$ reported for 0.2218 M solution of (2*S*,3*S*)-(−)-2,3-dimethylaziridine in heptane is multiplied by −1; see ref 31. [j] $[\alpha]_D$ reported for 3.2 M solution of (2*S*,3*S*)-*N*-chloro-2,3-dimethylaziridine in heptane is multiplied by −1; see ref 33.

An explicit evaluation of the sum over excited states in eq 1 can be avoided by noting that when $\omega_{ns} \gg \omega$ eq 1 can be simplified as[17]

$$\omega^{-1}\mathrm{G}'_{\alpha\beta} = -(h/\pi)Im\{\langle(\partial\psi_s/\partial F_\alpha)|(\partial\psi_s/\partial B_\beta)\rangle\} \quad (5)$$

Amos developed,[17] and implemented,[18] an approach for evaluating eq 5 by calculating the derivatives $(\partial\psi_s/\partial F_\alpha)$ and $(\partial\psi_s/\partial B_\beta)$ using the coupled perturbed Hartree−Fock method.[19] Equation 5 has been evaluated before[10] at the displaced nuclear geometries for calculating the vibrational Raman optical activity intensities. However, the application of eq 5 to optical rotations via eqs 1−4 has been undertaken only recently.[11,12]

Results and Discussion

Standard basis sets available in the CADPAC program[18] library were used. The geometries were optimized with the 6-31G* basis set.[20] Two different optical rotation calculations, one with the 631G* and another with the DZP basis set,[21] both using the 6-31G* optimized geometries, were undertaken and are reported in Tables 1 and 2. The specific rotations were calculated for the sodium D-line wavelength (589.3 nm). The three-dimensional structures of the molecules resulting from the geometry optimizations are displayed in Figures 1 and 2.

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Table 2. Ab Initio Theoretical and Experimental Optical Rotations for Unsymmetrically Substituted Aziridines and Azetidines

		optical rotation, $[\alpha]_D$		
		calcd		
molecule	confgrtn	631G*	DZP	expt
2-methylaziridine (*trans*)	(2*R*)	−13.2	−24.0[a]	+12.4[b]
2-methylaziridine (*cis*)	(2*R*)	+40.5	+67.5[a]	
N-chloro-2-methylaziridine (*trans*)[c]	(2*R*)	−83.7	−143	+94[d]
N-chloro-2-methylaziridine (*cis*)[c]	(2*R*)	+27.8	−23.3	−81[d]
2-methylazetidine (*trans*)	(2*S*)	22.9	−25.7	−3.05[e]
2-methylazetidine (*cis*)	(2*S*)	29.6	23.2	
N-chloro-2-methylazetidine (*trans*)	(2*S*)	+104	+107	−21.5[f]

[a] Here a larger 631G(ext) basis set was used in place of the DZP basis set. [b] $[\alpha]_D$ value reported for 1.5 M solution of (2*R*)-2-methylaziridine in $C2H_5OH$; ref 34. [c] A larger 631G(ext) basis set yielded $[\alpha]_D = -128$ and +34.6, respectively, for the trans and cis conformers. [d] $[\alpha]_D$ value reported for 0.8 M solution of (2*R*)-*N*-chloro-2-methylaziridine in nonane; ref 32. [e] $[\alpha]_D$ value reported for 3.7 M solution of (2*R*)-2-methylazetidine in nonane is multilied by −1; ref 35. [f] $[\alpha]_D$ value reported for 3.0 M solution of (2*R*)-*N*-chloro-2-methylazetidine in heptane is multiplied by −1; ref 35.

Substituted Cyclopropanes. The specific rotation predicted for (1*S*,2*S*)-*trans*-1,2-dimethylcyclopropane, assuming a refractive index of 1.0, is +9.94° with the 631G* basis set and +82.1° with the DZP basis set. The corresponding experimental value reported[22] for 0.5 M solution of (1*R*,2*R*)-*trans*-1,2-dimethylcyclopropane, in pentane, is −42°. Both calculations predict the correct relation between the sign of optical rotation and absolute configuration, but the 631G* prediction is nearly four times smaller and that of the DZP basis set is ~2 times larger. The specific rotation predicted for (2*R*,3*R*)-*trans*-2,3-dimethyl-1-methylenecyclopropane, assuming a refractive index of 1.0, is −64.3° with the 631G* basis set and +31.0° with the DZP basis set. The corresponding experimental value reported[23] for 1.72 M solution of (2*S*,3*S*)-*trans*-2,3-dimethyl-1-methylenecyclopropane, in CCl_4, is −57.6°. The prediction obtained with the 631G* basis set has the incorrect sign with roughly the same magnitude, but that obtained with the DZP basis set has the correct sign with a magnitude that is within a factor of 2 of the experimental value. Based on the comparison between the experimental and predicted rotations for the molecules discussed above, it appears that the DZP basis set is to be preferred over the 631G* basis set. The predicted specific rotations with the DZP basis set for (1*S*,2*S*)-*trans*-1,2-difluorocyclopropane and (1*S*,2*S*)-*trans*-1,2-dichlorocyclopropane, assuming refractive index of 1.0, are respectively +9.29° and +91.6°. The corresponding experimental rotations could not be found in the literature for these two cases.

Heterocyclic Ring Systems with Oxygen Atom in the Ring. The specific rotation predicted for (2*S*)-2-methyloxetane, using a refractive index[24] of 1.3913, is +26.4° with the 631G* basis set and +29.4° with the DZP basis set. The corresponding experimental value reported[25] for neat liquid of (2*S*)-2-methyloxetane is +33.5°. Here both calculations are in close agreement with the experimental value. In the case of (2*R*)-methyloxirane and (2*R*,3*R*)-*trans*-2,3-dimethyloxirane also the predicted rotations[11] were in reasonable agreement with the corresponding experimental rotations.

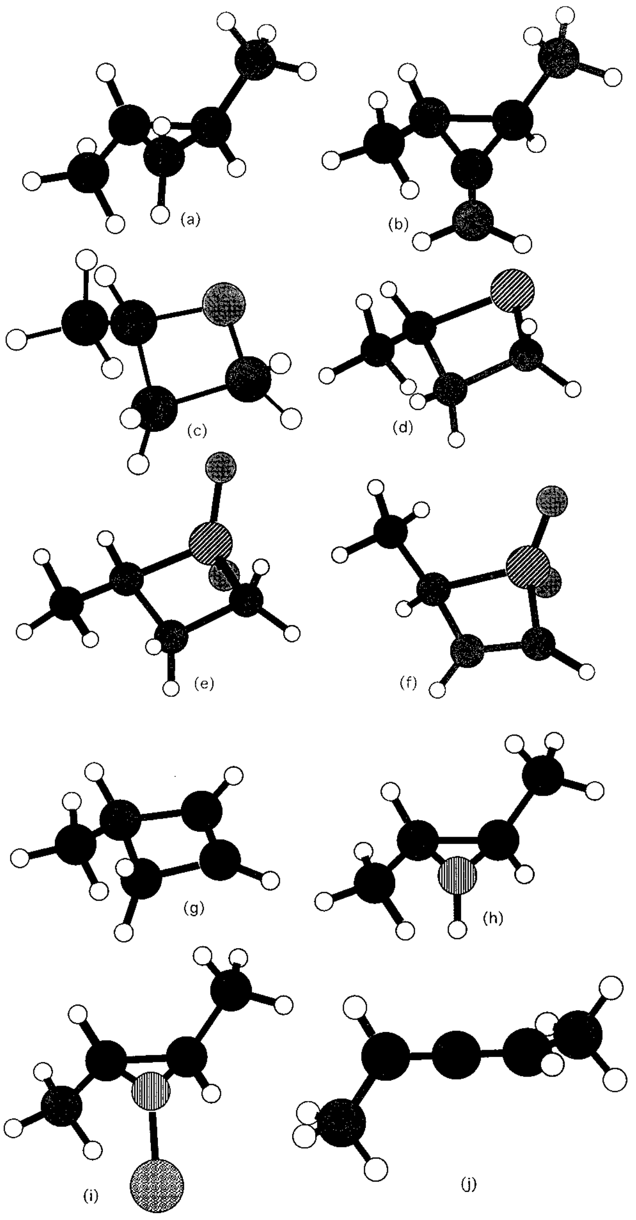

Figure 1. Ab initio geometries and absolute configurations, optimized with the 631G* basis set, for molecules in Table 1. (a) (1*S*,2*S*)-*trans*-1,2-dimethylcyclopropane; (b) (2*R*,3*R*)-*trans*-2,3-dimethyl-1-methylenecyclopropane; (c) (2*S*)-2-methyloxetane; (d) (2*S*)-2-methylthiitane; (e) (2*S*)-2-methylthietane-1,1-dioxide; (f) (4*R*)-4-methylthiete-1,1-dioxide; (g) (3*S*)-3-methylcyclobutene; (h) (2*R*,3*R*)-*trans*-2,3-dimethylaziridne; (i) (2*R*,3*R*)-*N*-chloro-*trans*-2,3-dimethylaziridine; and (j) (a*S*)-1,3-dimethylallene.

Heterocyclic Ring Systems with Sulfur Atom in the Ring. The specific rotation predicted for (2*S*)-2-methylthiitane, assuming a refractive index of 1.0, is −83.4° with the 631G* basis set and −148° with the DZP basis set. The corresponding experimental value could not be found for methylthiitane, but that reported[26] for 2.5 M solution of (2*S*)-2-propylthiitane in $CHCl_3$ is −133°. Assuming that the substitution of propyl group for the methyl group does not alter the specific rotation significantly, the DZP predicted optical rotation can be seen to be in close agreement with the experimental value. Similar

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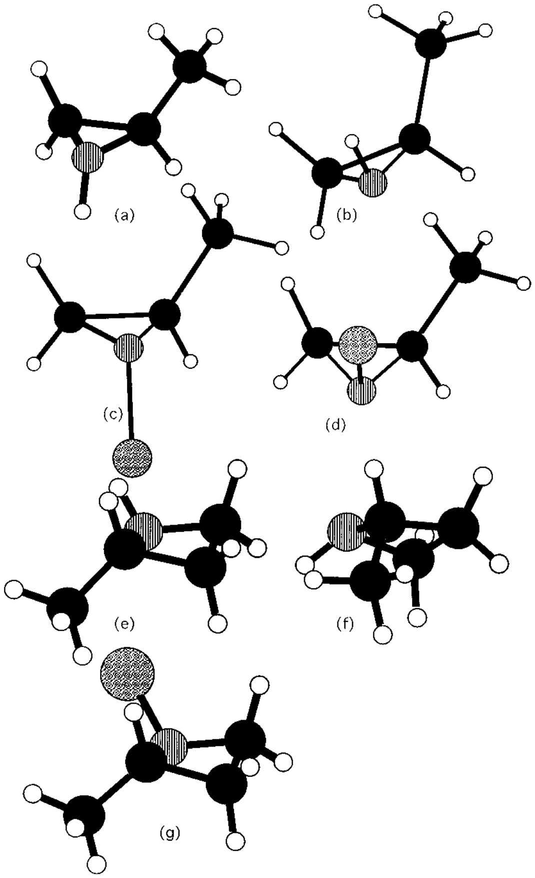

Figure 2. Ab initio geometries and absolute configurations, optimized with the 631G* basis set, for unsymmetrically substituted aziridines and azetidines: (a) (2*R*)-2-methylaziridine (*trans*); (b) (2*R*)-2-methylaziridine (*cis*); (c) (2*R*)-*N*-chloro-2-methylaziridine (*trans*); (d) (2*R*)-*N*-chloro-2-methylaziridine (*cis*); (e) (2*S*)-2-methylazetidine (*trans*); (f) (2*S*)-2-methylazetidine (*cis*); (g) (2*S*)-N-chloro-2-methylazetidine (*trans*).

observation is also noticed for (2*S*)-2-methylthiitane-1,1-dioxide. The specific rotation predicted for (2*S*)-2-methylthiitane-1,1-dioxide, using a refractive index[27] of 1.4689, is −8.37° with the 631G* basis set and −29.4° with the DZP basis set. The experimental rotation reported[27] for 9.5 M solution of (2*R*)-2-methylthiitane-1,1-dioxide in C_2H_5OH is +21.0°. For (*S*)-methylthiirane and (2*S*,3*S*)-*trans*-2,3-dimethylthiirane also the predicted optical rotations[11] were in reasonable agreement with the corresponding optical rotations. In the case of (4*R*)-4-methylthiete-1,1-dioxide, which has a double bond in the ring, both calculations predicted somewhat larger optical rotation than was observed: the predicted rotations, with a refractive index[27] of 1.4813, being −41.3° with 631G* basis set and −76.8° with DZP basis set, while the experimental rotation[27] for 5.99 M solution of (4*R*)-4-methylthiete-1,1-dioxide in $CHCl_3$ being −21.2°.

Carbon Ring Systems with a Multiple Bond. 3-Methylcyclobutene provides a representative of chiral carbon ring molecules with a multiple bond in the ring. The specific rotation predicted for (3*S*)-3-methylcyclobutene, with a refractive index[28] of 1.3968, is −95.7° with the 631G* basis set and −176° with the DZP basis set. The experimental value reported[28] for neat liquid (3R)-3-methylcyclobutene with 66% optical purity is 116.24, which when scaled to 100% optical purity gives +176°. Thus while the prediction obtained with the 631G* basis set is nearly two times smaller, that obtained with the DZP basis set is in pleasing agreement with the experimental optical rotation. (2*S*,3*S*)-*trans*-2,3-Dimethyl-1-methylenecyclopropane, considered earlier, has a multiple bond external to the carbon ring. For two other molecules, namely (3*R*)-3-methylcyclopentanone and (3*R*)-3-methylcyclohexanone also, both of which have a multiple bond external to the carbon ring, the predicted optical rotations[11] were in reasonable agreement with the corresponding experimental optical rotations.

Molecules Devoid of Chiral Centers. This class of molecules provides a useful test for the predictions, as there are no chiral centers in the molecule and the establishment of absolute configuration is not usually straightforward. Chiral molecules such as H_2O_2 provide the simplest examples of this category but the enantiomers of such simple molecules are not experimentally resolvable, so the experimental data do not exist for such molecules. Molecules such as substituted chiral biphenyl are too large for us to handle at the present time in the ab initio geometry optimizations. However an excellent example of this category is 1,3-dimethylallene, because the enantiomers of this molecule have been resolved, experimental optical rotations reported,[29] and this molecule is simple enough for undertaking ab initio predictions. The specific rotation predicted for (a*S*)-1,3-dimethylallene, with an assumed refractive index of 1.4190 (same as that for 3,3-dimethylallene[30]), is +108° with the 631G* basis set and +207° with the DZP basis set. The experimental value reported[29] for neat liquid (a*R*)-1,3-dimethylallene with 7% optical purity is −15.9, which when scaled to 100% optical purity gives −227°. The DZP predicted rotation is in good agreement with the experimental value, while the 631G* predicted value is nearly two times smaller.

Heterocyclic Ring Systems with Nitrogen Atom in the Ring. Here we consider aziridines and azetidines and divide them into two classes, symmetrically substituted and unsymmetrically substituted, as described below.

First let us consider the symmetric aziridines. The specific rotation predicted for (2*R*,3*R*)-*trans*-2,3-dimethylaziridine, with a refractive index[31] of 1.4076, is +44.6° with the 631G* basis set and +46.2° with the DZP basis set. The experimental value reported[31] for 0.2218 M solution of (2*S*,3*S*)-*trans*-2,3-dimethylaziridine in heptane is −103.8°. The predicted sign is correct in both calculations, but the predicted magnitude in both cases is more than two times smaller than the experimental value. In the case of (2*R*,3*R*)-N-chloro-*trans*-2,3-dimethylaziridine the specific rotation predicted, with assumed refractive index of 1.4120 (same as that of methylaziridine[32]), is −42.6° with the 631G* basis set and −97.0° with the DZP basis set. The experimental value reported[33] for 3.2 M solution of (2*S*,3*S*)-N-chloro-*trans*-2,3-dimethylaziridine in heptane is +16.8°. Here again the predicted sign is correct in both calculations, but the predicted magnitude in both cases is larger than the experimental value by ∼3 to 6 times. Thus for both of the symmetrically substituted aziridines, predictions provide the correct relation between the sign of optical rotation and absolute configuration, but the predicted magnitudes differ from the experimental magnitudes.

In the case of unsymmetrically substituted aziridines and azetidines (Table 2) one has to consider both trans and cis conformers (here trans and cis refer to the N−H group with

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respect to a substitutent on ring carbon), and it is known that the population of the trans conformer dominates that of the cis conformer. The specific rotation predicted for the trans conformer of (2*R*)-2-methylaziridine, with a refractive index[32] of 1.4120, is −13.2° with the 631G* basis set and −24.0° with the 631G(ext) basis set. The specific rotation predicted for the cis conformer of (2*R*)-2-methylaziridine, with a refractive index[32] of 1.4120, is +40.5° with the 631G* basis set and +67.5° with the 631G(ext) basis set. The 631G* energy difference between these conformers predicts a population of 74% for trans and 26% for cis conformer. Then the population weighted optical rotation for (2*R*)-2-methylaziridine would be +0.76° at the 631G* level and −0.21° at the 631G(ext) level. The experimental value reported[34] for 1.5 M solution of (2*R*)-2-methylaziridine in C_2H_5OH is +12.4°. Since the calculations predict extremely small optical rotation with differing signs, it seems important to establish the precise population of the conformers. In the case of N-chloro-2-methylaziridine, the trans and cis conformers were experimentally resolved, so individual comparisons, instead of the population weighted values, can be made. The specific rotation predicted for the trans conformer of (2*R*)-N-chloro-2-methylaziridine, with assumed refractive index of 1.4410 (same as that of N-chloro-2-methylazetidine[35]), is −83.7° with the 631G* basis set and −143° with the DZP basis set. Both predictions are in disagreement with the experimental value[32] of the trans conformer, which for 0.8 M solution of (2*R*)-N-chloro-2-methylaziridine in nonane is +94°. The specific rotation predicted for the cis conformer of (2*R*)-N-chloro-2-methylaziridine, with a refractive index of 1.4410, is +27.8° with the 631G* basis set and −23.3° with the DZP basis set. The experimental value[32] for the cis conformer, as 0.8 M solution of (2*R*)-N-chloro-2-methylaziridine in nonane, is −81°. The 631G* prediction is in disagreement with the experimental value, but the DZP prediction has the correct sign, although the predicted magnitude is nearly four times smaller. In the case of 2-methylazetidine the specific rotation predicted for the trans conformer of (2*S*)-2-methylazetidine, with a refractive index[35] of 1.4208, is +22.9° with the 631G* basis set and −25.7° with the DZP basis set. The specific rotation predicted for the cis conformer of (2*S*)-2-methylazetidine, with a refractive index of 1.4208, is +29.6° with the 631G* basis set and +23.2° with the DZP basis set. The 631G* energy difference between these conformers predicts a population of 89% for trans and 11% for cis conformer. Then the population weighted optical rotation for (2*S*)-2-methylazetidine would be +23.6° at the 631G* level and −20.3° at the DZP level. The experimental value reported[35] for (2*R*)-2-methylazetidine is +3.05°. The optical rotation sign predicted by the 631G* basis set is incorrect, but that predicted by the DZP basis set is correct, although the magnitude is ∼7 times large. The disagreement between predictions and experimental observation noted earlier for the trans conformer of N-chloro-2-methylaziridine is also apparent for the trans conformer of N-chloro-2-methylazetidine. The specific rotation predicted for the trans conformer of (2*S*)-N-chloro-2-methylazetidine, with a refractive index[35] of 1.4208, is +104° with the 631G* basis set and +107° with the DZP basis set. The experimental value[35] for 3.0 M solution of (2*R*)-N-chloro-2-methylazetidine in heptane is +21.5°, and it is assumed that the trans conformer is predominant.[35] Both calculations predict the wrong sign and the incorrect magnitude in this case.

Conclusions

From the results presented in the previous section it can be noted that the relation between the sign of optical rotation and absolute configuration has been correctly predicted for (a) substituted cyclopropanes; (b) heterocyclic ring systems with oxygen atom in the ring; (c) heterocyclic ring systems with sulfur atom in the ring; (d) carbon ring systems with a multiple bond; and (e) 1,3-dimethylallene, a molecule devoid of chiral centers. Similar conclusion was reached for chiral fluorinated ethers and bromochlorofluoromethane in the earlier investigations.[11,12]

This positive conclusion should be noted along with the limitation seen for some of the unsymmetrically substituted aziridines and azetidines. The predictions obtained for this class of molecules, especially for the trans conformers of N-chloro-2-methylaziridine and N-chloro-2-methylazetidine, are less than satisfactory, so caution should be exercised for molecules related to this class. One reason for the disappointing results here might be that the excited electronic states are not adequately described at the 631G* and DZP levels. Further investigations would be needed to gain insight into the disagreements between predicted and observed rotations for this class of molecules.

Both the signs and magnitudes of optical rotations predicted with the DZP basis set are generally in better agreement, than are those obtained with the 631G* basis set, with the corresponding experimental data. It is to be noted however that the magnitudes of the experimental optical rotations depend on the solvent used. The solvent effect is not incorporated into the present calculations. The predicted optical rotation magnitudes correspond to isolated molecules and should therefore be compared with the vapor phase optical rotations. But the vapor phase optical rotations are rarely, if ever, measured. Despite this limitation, the comparison between the predicted and experimental optical rotation magnitudes can be seen to be favorable. These observations reflect the reliability of the use of ab initio optical rotations to establish the absolute stereochemistry. The ab initio optical rotation calculations are now computationally much less demanding than the other forms of optical activity (ECD, VCD, and VROA), so a practicing chemist can greatly benefit from these observations when the quantum mechanical programs implementing the optical rotation calculations become widely available.

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