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Theoretical Analysis of Optical Rotatory Power of Methylcyclohexanone with Treatment of Conformational Equilibria

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Optical rotational strength for the n-π^* transition of (*R*)-3-methylcyclohexanone is calculated by the CNDO/2 and INDO methods and compared with the observed values at 81 and 300 K, taking account of conformational equilibria. The conformer species are chosen so that they have minimal potential energies, the potential energy surface being estimated with a non-bonded interaction approximation. Excited state wave functions are improved by a model potential method. The ratio of the rotational strengths at 81 and 300 K, each of them being calculated as a statistical average of the rotational strengths of four conformers, is in good agreement with the corresponding observed value.

In the course of recent advances in quantum chemical approach for the prediction of optical rotatory power of optically active molecules, there have been brought forward several questions to answer; interpretation of observed circular dichroism spectra which are usually taken in solution, reasonable guess of molecular conformations, accuracy of ground and excited state functions, estimation of two-center (interatomic) matrix elements of the electric and magnetic dipole moment integrals, and so on.

Of all such problems the most important seems to be those about the first two, on which recent measurements[1] of circular dichroism spectra over a wide range of temperature have thrown the ray of hope for the settlement of the matter. That is, the rotational strengths of most optically active ketones increase as temperature goes down. Under the circumstances, one has no choice but to view that there must be several types of conformers mixed in a single solution, distributing according to the Boltzmann law, and giving one a temperature-dependent, statistically averaged rotational strength for a specific electronic transition. This view was first adopted by Moscowitz *et al.*[2] for the interpretation of thermodynamic data of (*R*)-*trans*-2-chloro-5-methylcyclohexanone, though they confined themselves only to a treatment of a two-conformer equilibrium. In the present study, we follow the above viewpoint in a comparison of experimental and theoretical optical rotatory powers of (*R*)-3-methylcyclohexanone, taking account of a multi-conformer equilibrium.

There is no definite way to guess what types of conformers effectively contribute to the mixing and what molecular geometry each conformer has. Among several procedures for conformational analysis of flexible molecules, we turn our attention to a classic model of interatomic interactions, *i.e.*, non-bonded and/or van der Waal's interactions, plus tortional interactions, which has been successfully applied to a number of saturated compounds by many authors.[3,4] Though the model is too simple to predict the precise temperature-dependent rotational strength of (*R*)-3-methylcyclohexanone, we have found after trying several other means that it is the only reliable way to guess the conformational (potential) energy surface of conformers.

As for the absolute magnitudes of rotational strengths of free molecules, there have been reported a good number of molecular orbital calculations, in particular cyclohexanone methyl derivatives have been most carefully investigated.[5] Good excited state wave functions are required in a calculation of rotational strength, and a usual procedure for improving approximate state functions is to invoke a configuration interaction (CI). Since the practical CI procedure for the calculation of matrix elements of the electric and magnetic dipole moments is rather complicated and troublesome, we shall adopt a model potential method in order to improve virtual orbitals to be used in a single-determinantal excited state functions.

Methods of Calculation

As mentioned above, we start from the viewpoint that the proper method for comparison of experimental and theoretical results would be to use a Boltzmann distribution among non-interacting conformers in order to obtain an average value for the rotational strength of the electronic transition under consideration at temperature T:

$$[R^l]^T_{\mathrm{av}} = \frac{\sum\limits_i [\mathrm{R}^l_i]\exp(-E_i/kT)}{\sum\limits_i \exp(-E_i/kT)} \tag{1}$$

where $[R^l_i]$ is the reduced rotational strength in the lth transition of conformer i and has the form

$$[R^l_i] = 1.08 \times 10^{40}\,\mathrm{Im}(\boldsymbol{\mu}^l \cdot \boldsymbol{m}^l), \tag{2}$$

$\boldsymbol{\mu}^l$ and $\boldsymbol{m}^l$ being the electric and magnetic dipole moments associated with transition l, and E_i is the conformational energy of conformer i measured from that of the most stable conformer.

An estimation of the value E_i is most difficult. An *ab initio* calculation of a precise potential curve associated with a conformational change is laborious, whereas a semi-empirical molecular orbital method seems no good to the estimation of such small energy differences as several kcal/mol among conformers. We therefore adopted as a measure of E_i the potential energies due to a non-bonded interaction between atoms and an internal rotation about a single bond. The former is represented by the Lennard-Jones "6—12" potential

$$U_{ij} = \frac{d_{ij}}{r_{ij}^{12}} - \frac{e_{ij}}{r_{ij}^{6}} \tag{3}$$

where d_{ij} and e_{ij} are the constants specific for atoms and assume to take the values given by Scott and Scheraga,[6] r_{ij} being the non-bonded interatomic distance in Å. The potential energy for a single internal rotation is given by

$$U_{\text{rot}} = \frac{1}{2}C(1-\cos 3\phi) \tag{4}$$

where C is the height of the potential peaks above the potential valleys and takes the values determined by Scott and Scheraga. We shall calculate U_{rot} for all the possible internal rotation arising from the change of the dihedral angles $\phi(3)$ and $\phi(5)$ (*vide infra*). An electrostatic (coulomb) interaction is neglected since there is only one polar bond in the molecule under consideration and such an interaction is very small.

The molecular orbitals used for the calculation of $[R_i^l]$ are obtained from the CNDO/2 and INDO methods. All the parameters involved are the same as those proposed by the original authors.[7] In order to obtain better excited state wave functions, we adopted Huzinaga and Arnau's model potential method.[8] The method uses the following Hartree-Fock operator[9] for a "singlet" excitation of one electron from the ith orbital

$$F_i = H + \sum_{j\neq i}(2J_j-K_j) - J_i + 2K_i \tag{5}$$

where J and K are the usual coulomb and exchange operators respectively, and $-J_i+2K_i$ is a pseudopotential which plays a significant part to improve virtual orbitals. The method has been shown to have the advantage of making an excited state calculation easier than the usual CI procedure.

The two-center (interatomic) terms of the electric and magnetic dipole moments are included in calculations of $[R_i^l]$ together with the one-center terms.[10] The dipole velocity formulation is adopted instead of the dipole length formulation. As pointed out by several writers,[11,12] the inclusion of the two-center terms in CNDO and INDO-type calculations is incompatible with the use of the zero differential overlap approximation. Therefore, CNDO and/or INDO basis sets should be transformed into deorthogonalized basis sets under the assumption that the CNDO and INDO basis are represented by Löwdin's orthogonalized atomic orbitals. We follow the recipe for deorthogonalization given by Imamura *et al.*[12]

In short, the molecular orbitals used for the purpose of comparison are divided into the following four:

Method I: CNDO/2 and/or INDO MO's without any modification.

Method II: MO's deorthogonalized.

Method III: MO's improved by the model potential method.

Method IV: MO's improved by the model potential method and deorthogonalized.

Results and Discussion

Figure 1 shows the molecular geometry of (*R*)-3-methylcyclohexanone proposed by Pao and Santry.[13] We first constructed a large number (about 200) of conformers by changing the dihedral angles $\phi(3)$ and $\phi(5)$ shown in Fig. 2, all the CCC angles being fixed

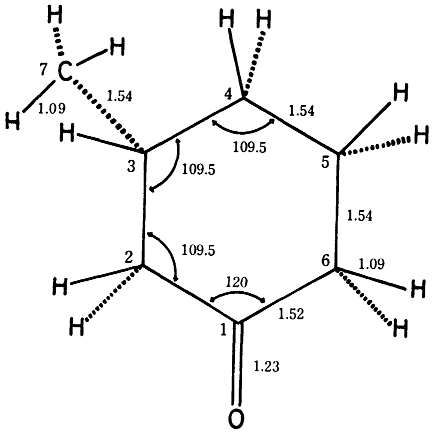

Fig. 1. Molecular geometry of (*R*)-3-methylcyclohexanone; bond lengths are given in Å and angles in degrees.

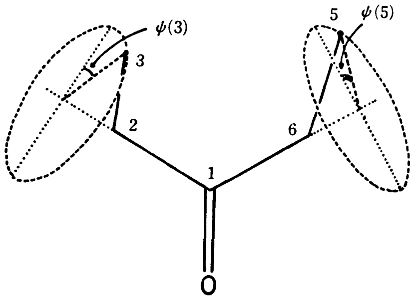

Fig. 2. Dihedral angles $\phi(3)$ and $\phi(5)$ in (*R*)-3-methylcyclohexanone.

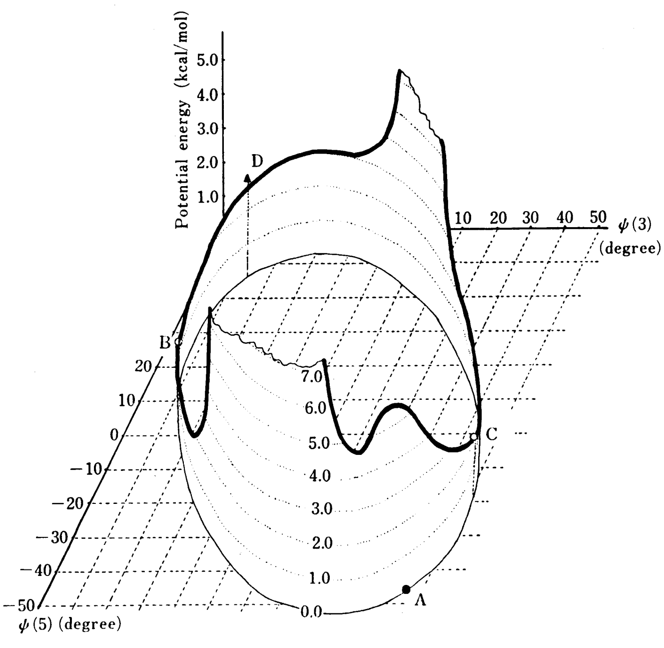

Fig. 3. Bird's-eye view of the potential surface for (*R*)-3-methylcyclohexanone.
A: Chair form with equatrial methyl; D: chair form with axial methyl; B, C: conformers corresponding to two minima of the surface.

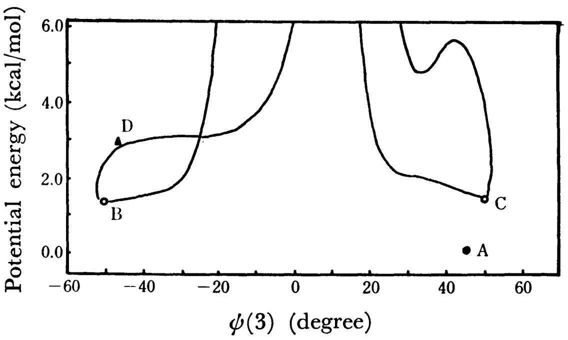

Fig. 4. Projection of the potential surface onto the $\phi(3)$-energy plane. A, B, C, and D are the same as in Fig. 3.

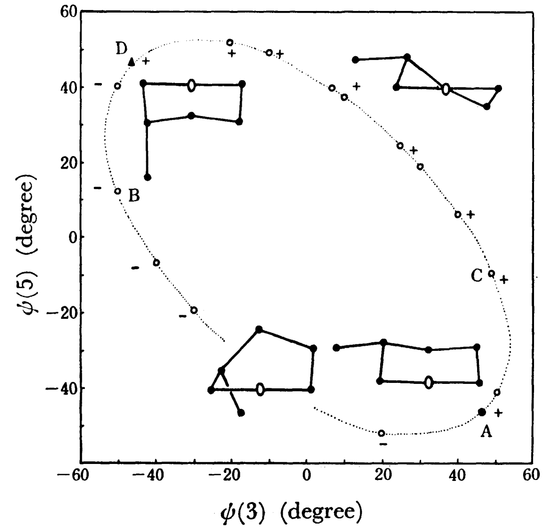

Fig. 5. Projection of the potential surface onto the plane of two dihedral angles, $\phi(3)$ and $\phi(5)$. + and − denote sings of rotational strength and A, B, C, and D are the same as in Fig. 3.

as in Fig. 1, and calculated the total non-bonded potential energies $\sum(U_{ij}+U_{\mathrm{rot}})$ as a function of $\phi(3)$ and $\phi(5)$. Let the value of $\phi(3)$ be zero when atom C_3 is in the *trans* position with respect to the C=O bond and positive for the counter-clockwise rotation of the C_2–C_3 bond.

The results are illustrated in Fig. 3, where the potential energy is measured from that for the regular chair-form conformer with the equatrial methyl group (A in the figure). No conformer was found to have a lower potential energy than A, which then corresponds to a singular point in the potential energy surface. Thus, the regular chair-form conformer having the equatrial methyl group is computed out to be most stable, as might be expected. On the other hand, the potential energy of the regular chair-form conformer having the axial methyl group, D, comes to the neighborhood of the potential surface of the boat-forms. Figure 4 is a projection of the potential surface onto the $\phi(3)$-energy plane. There are found two potential minima, the corresponding conformers being called B and C.

The projection of the potential surface onto the plane of two dihedral angles $\phi(3)$ and $\phi(5)$ is illustrated in Fig. 5 which shows a correlation between signs of the calculated rotational strengths and the species of conformers. Each open circle corresponds to a selected conformer for which the rotational strength has been calculated and its sign is marked as plus or minus. For reference, some representative conformers are illustrated roughly at their proper positions. These calculated signs of rotational strength agree with those predicted by the octant rule, if it assumes to be applied even for a boat and/or twist boat-form conformer. However, in conflict with the octant rule, the calculated rotational strength for the regular chair-form conformer with the axial methyl group has a positive sign.

In Table 1 is listed a part of the calculated results for rotational strength for the n-π^* transition of (*R*)-3-methylcyclohexanone. Conformers B and C are chosen because they have the potential energies that correspond to minima of the potential surface (*vide supra*). The results for some other conformers of boat-form are also listed for reference.

With these calculated rotational strengths and potential energies of conformers A, B, C, and D, we calculate from Eq. 1 the statistical average of the rotational strength for the n-π^* transition of (*R*)-3-methylcyclohexanone at 300 and 81 K. The results are shown in Tables 2 together with the values Δ defined by

$$\Delta = \frac{[R]^{81}_{\mathrm{av}} - [R]^{300}_{\mathrm{av}}}{[R]^{300}_{\mathrm{av}}} \times 100. \qquad (6)$$

There can be seen in Table 2 a quite good agreement between the calculated and observed Δ values, though the absolute values of the predicted rotational strengths

Table 1. Calculated rotational strengths of conformers of (*R*)-3-methylcyclohexanone[a)]

Conformer	Angle (degree)		CNDO/2				INDO			
	$\phi(3)$	$\phi(5)$	I	II	III	IV	I	II	III	IV
A	46.02	−46.02	9.118	15.809	8.133	12.410	10.927	20.539	9.168	13.734
B	−50.00	12.49	−74.396	−100.294	−51.709	−56.239	−56.230	−75.654	−35.010	−34.204
C	48.50	−8.66	71.583	97.313	53.000	58.115	55.806	77.422	36.852	38.274
D	−46.02	46.02	16.462	20.585	13.538	15.094	9.430	10.453	7.959	8.224
Boat axial	46.02	−46.02	7.223	9.093	6.084	7.020	6.448	9.060	4.794	5.734
Boat equatrial	−46.02	46.02	−17.216	−25.673	−12.241	−14.833	−14.993	−23.582	−10.130	−11.915
Twist boat	24.67	24.67	41.126	43.017	41.855	39.601	34.151	36.826	29.937	24.600

a) Observed rotational strengths are +1.78 and +2.34 at 300 and 81 K, respectively.

TABLE 2. TEMPERATURE-DEPENDENT ROTATIONAL STRENGTHS OF (R)-3-METHYLCYCLOHEXANONE CALCULATED WITH NON-BONDED INTERACTION ENERGY AS CONFORMATIONAL ENERGY

Temperature	CNDO/2				INDO				Exptl.[a]
	I	II	III	IV	I	II	III	IV	
300 K	5.505	10.226	5.482	8.766	7.416	14.683	6.620	10.351	1.78
81 K	9.118	15.809	8.152	12.410	10.927	20.539	9.168	13.734	2.34
Δ(%)[b]	65.64	54.59	48.71	41.58	47.34	39.88	30.01	32.68	31.5

a) Ref. 1. b) Defined by Eq. 6 of the text.

are considerably larger than the observed value (see Table 1 also). Methods III and IV with INDO yield better results, so that an improvement of virtual orbitals such as the present one seems to be prerequisite for calculations of this type. However, we cannot say for certain about the importance of the effect of deorthogonalization which has been demonstrated by other investigators.[12] We shall report elsewhere that a calculation without deorthogonalization leads to incorrect results with respect to a sign of the rotatory strength of (R)-3-methylcyclohexylidene-malononitrile.[14] The calculated weights of conformers A, B, C, and D are 82.91, 9.30, 7.11, 0.68%, respectively, at 300 K with Method IV. At 81 K with the same method, the weight of conformer A is 100%.

The above-mentioned calculations are based on the assumption that the potential surface obtained from the consideration of non-bonded interactions can well describe the internal energy profile of the system. What about a situation, if we use as E_i the sum of the electronic energy calculated by the molecular orbital methods and the potential energy due to the non-bonded interactions? As can be seen in Table 3, the results obtained are rather unsatisfactory. This may partly be attributed to the present inconsistent procedure which uses the same conformers as in the previous case (A, B, C, and D). The reason why proper conformers are not used is simply because minima of the energy surface in this case have hardly been found.

Lastly, there still remains a question: Is the sign of the rotational strength of conformer D definitely positive? There has been no calculation reported that conformer D has a negative sign in accordance with the ketone octant rule. We have no mind to challenge the octant rule and simply want to find out a relationship between a sign of rotatory strength and a molecular conformation. We have found that the rotational strength gradually decreases as the C_3–C_7 bond rotates in the plane which contains the C_3–C_7 bond and is perpendicular to the $C_2C_3C_4$ plane (Fig. 6). The numerical values obtained are listed in Table 4, where $\delta\theta$ denotes the deviation of the dihedral angle defined above, $\delta\theta=0$ being the axial position of bond C_3–C_7 with respect to bond C_1–C_2 in conformer D. In order to get the sign to be negative, the axial methyl group must rotate by about 20 degrees. This request, on the other hand, inflicts an energy loss of about 0.2 eV (see the last column of Table 4) and is rather unlikely. Thus, in so far as the above estimation is correct, a sign of the rotational strength of conformer D will probably be positive as the present and some other authors predict. It should be noted that the conclusion here is only tentative since we cannot say definitely about the accuracy of the total energies of conformers under consideration. There may be cases that a total energy favors reorientation of axial

TABLE 3. TEMPERATURE-DEPENDENT ROTATIONAL STRENGTHS OF (R)-3-METHYLCYCLOHEXANONE CALCULATED WITH THE SUM OF ELECTRONIC ENERGY AND NON-BONDED INTERACTION ENERGY AS CONFORMATIONAL ENERGY

Temperature	INDO			
	I	II	III	IV
300 K	10.885	20.473	9.140	13.695
81 K	10.904	20.505	9.151	13.711
Δ(%)[a]	0.17	0.16	0.12	0.12

a) Defined by Eq. 6.

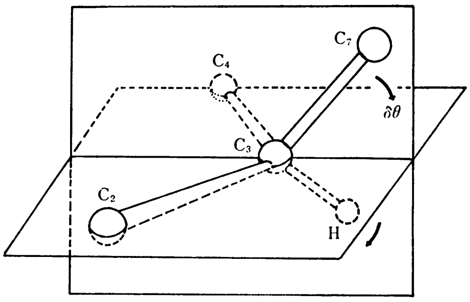

Fig. 6. Inclination angle of the methyl group, $\delta\theta$.

TABLE 4. EFFECT OF INCLINATION ANGLE ($\delta\theta$) OF METHYL GROUP ON ROTATIONAL STRENGTH OF CHAIR-FORM (R)-3-METHYLCYCLOHEXANONE WITH AXIAL METHYL (CONFORMER D)

$\delta\theta$[a] (degree)	INDO				Total energy (eV)
	I	II	III	IV	
0.0	9.430	10.453	7.959	8.224	−2039.219
5.0	7.594	7.539	7.764	8.073	−2039.332
10.0	4.771	2.769	7.002	7.004	−2039.282
20.0	−2.530	−10.430	4.413	2.747	−2038.996
30.0	−10.092	−25.710	0.786	−4.561	−2038.480

a) Clockwise rotation of bond C_3-C_7 in the plane which contains bond C_3-C_7 and is perpendicular to the $C_2C_3C_4$ plane. $\delta\theta$ is taken to the zero at the axial position of bond C_3-C_7 with respect to bond C_1-C_2.

methyl groups in some alicyclic ketones. The ketone octant rule will hold properly for such molecules.

In order to see what happens if we start from somewhat different molecular geometry, we have carried out a copy of the above calculation with the geometry of (*R*)-3-methylcyclohexanone proposed by Moffitt *et al.*[15] The overall results however were not very good; *e.g.*, the value of Δ was computed to be about 13.

It is concluded that consideration of the statistical population of conformers is indispensable for accurate understanding of rotational strength data of flexible optically active molecules.

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