J. Am. Chem. Soc. 1983, 105, 6406–6410

Coupled Oscillator Interpretation of the Vibrational Circular Dichroism of Several Dicarbonyl-Containing Steroids

Usha Narayanan and T. A. Keiderling*

Contribution from the Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60680. *Received March 21, 1983*

Abstract: Vibrational circular dichroism spectra of several steroidal compounds containing two carbonyl groups on six-membered rings have been measured in the C=O stretching region. The results have been compared with the predictions of the degenerate coupled oscillator model. The sign and shape of the predicted spectra agree with the observed results in all but one case. The magnitudes agree to within a factor of 2, with two exceptions. Attempts made to correct the theory for misalignment of dipoles and nondegeneracy of the oscillators are discussed. In general, such corrections did not lead to an improved agreement. Other sources of error are discussed.

Introduction

In recent years, the measurement of circular dichroism of chiral molecules has been extended well into the infrared region.[1] The availability of vibrational circular dichroism (VCD) data for a wide variety of molecular vibrational transitions has rekindled promise of new experimental data of use for studies of molecular conformation or configuration.[2] Fulfillment of this potential is dependent on development and testing of a reliable theoretical model for correlation of structure and spectra. Many such models of varying complexity have been proposed.[3-7] In this paper we shall address the effectiveness of the simplest of these, the coupled oscillator model as formalized by Holzwarth and Chabay (HC).[3]

In their development, HC addressed the chirality and subsequent VCD of two identical, achiral dipolar oscillators μ_a and μ_b, that are mutually oriented in a chiral manner (noncoplanar). The lowest energy transitions of this system are to a pair of coupled excited states, ψ^+ and ψ^-, where $\psi^{\pm} = \phi_a{}^0\phi_b{}^1 \pm \phi_a{}^1\phi_b{}^0$ and ϕ^0,ϕ^1 represent the ground and first excited state of the single oscillator. The rotational strengths that result in first order for these transitions are equal in magnitude but opposite in sign. If these coupled states are not degenerate, a sigmoidal VCD line shape will result whose sign and magnitude are directly dependent upon geometrical parameters. Because of the chiral nature of their coupling, ψ^+ and ψ^- will not be exactly degenerate and, at minimum, will be perturbed by the electrostatic dipolar coupled interaction (or exciton effect). Subsequent workers have noted that both local chirality and nondegeneracy could be included in a coupled oscillator theory and have, somewhat incompletely, dubbed the simpler version of HC to be the degenerate coupled oscillator (DCO) model.[8]

Previously, we have applied the DCO model to the O—H and C=O stretching vibrations in dimethyl tartrate[9,10] and C=O vibrations in trans-substituted cyclopropanes[11] in an attempt to determine the relative geometry of those oscillators. In these cases, if the assumed geometries were correct, the oscillators were indeed degenerate, and the theoretical and experimental results were in satisfactory agreement. The DCO model also has been extended to polymeric systems[2,12] and has shown to agree with experimental VCD for the amide I (C=O stretch) vibration of those polypeptides having an α-helical secondary structure.[13,14]

In this paper, we present the VCD in the C=O stretching region of several steroidal compounds which contain two six-member-ring ketone carbonyls. These molecules were chosen to provide a variety of angles and interdipolar separations on a rigid framework[15] for two near-degenerate, strong dipolar oscillators. Evaluation of the ability of the DCO model to successfully predict the observed VCD of these transitions should help us determine the conditions in which the DCO model will be useful for structure–spectra correlations. Similar application of the coupled oscillator approach (there termed "exciton chirality") to the electronic CD of these systems has been quite successful.[16] VCD of an unsaturated steroidal ketone in this region has also been reported[17] and compared with predictions for a nondegenerate coupled oscillator.[8a]

Experimental Section

3,6-Dioxo-5α-cholestan (α36), 3,6-dioxo-5β-cholanic acid methyl ester (β36), 3,7-dioxo-5β-cholanic acid methyl ester (β37), 3,12-dioxo-5β-cholanic acid (β312), 7,12-dioxo-5β-cholanic acid (β712), 3α-hydroxy-7,12-dioxo-5β-cholanic acid (β712H), and 3-oxo-5β-cholanic acid were obtained from Steraloids, Inc., dissolved, filtered through activated charcoal, and recrystallized once from $CHCl_3$. They were then studied without further purification in $CHCl_3$ solution. Their structures are indicated schematically in Figure 1. VCD and absorption spectra were obtained on our previously detailed instrument.[1a] $CHCl_3$ solutions of acetone and, in some cases, methyl acetate were prepared to have the same absorbance in the C=O stretching region as found for the above samples. VCD of these achiral solutions were run after each steroid VCD experiment and were used as baselines. The instrument was constantly flushed with nitrogen gas to reduce interfering atmospheric H_2O absorption and thereby improve the VCD baseline. Four to eight scans of VCD with a resolution of 11 cm^{-1}, time constant 10 s, sample concentration of about 0.025 M, and path length of 0.035 cm were averaged for each sample and plotted with the appropriate baseline subtracted.

---

(1) Reviews of VCD: (a) Keiderling, T. A. *Appl. Spectrosc. Rev.* **1981**, *17*, 189. (b) Nafie, L. A. In "Vibrational Spectra and Structure"; Durig, J. R. Ed.; Elsevier: New York, 1981; Vol. 10. (c) Stephens, P. J.; Clark, R. In "Optical Activity and Chiral Discrimination"; Mason, S. F. Ed.; Reidel: Dortrecht, 1979. (d) Nafie, L. A.; Diem, M. *Acc. Chem. Res.* **1979**, *12*, 296.

(2) Deutsche, C. W.; Moscowitz, A. *J. Chem. Phys.* **1968**, *49*, 3257; **1970**, *53*, 2630.

(3) Holzwarth, G.; Chabay, I. *J. Chem. Phys.* **1972**, *57*, 1632.

(4) Schellman, J. A. *J. Chem. Phys.* **1973**, *58*, 2882; **1974**, *60*, 343.

(5) Abbate, S.; Laux, L.; Overend, J.; Moscowitz, A. *J. Chem. Phys.* **1981**, *75*, 3161.

(6) Walnut, T. H.; Nafie, L. A. *J. Chem. Phys.* **1977**, *67*, 1501. Nafie, L. A.; Walnut, T. H. *Chem. Phys. Lett.* **1977**, *49*, 441.

(7) (a) Marcott, C. A. Ph.D. Thesis, University of Minnesota, 1979. (b) Faulkner, T. R.; Marcott, C.; Moscowitz, A.; Overend, J. *J. Am. Chem. Soc.* **1977**, *99*, 8160. (c) Craig, D. P.; Thirunamachandran, T. *Mol. Phys.* **1978**, *35*, 825.

(8) (a) Faulkner, T. R. Ph.D. Thesis, University of Minnesota, 1976. (b) Marcott, C.; Faulkner, T. R.; Overend, J.; Moscowitz, A. *J. Am. Chem. Soc.* **1978**, *100*, 5262.

(9) Keiderling, T. A.; Stephens, P. J. *J. Am. Chem. Soc.* **1977**, *99*, 8061.

(10) Su, C. N.; Keiderling, T. A. *J. Am. Chem. Soc.* **1980**, *102*, 511. Su, C. N., Ph.D. Thesis, University of Illinois—Chicago Circle 1982.

(11) Heintz, V. J.; Keiderling, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 2395.

(12) Schellman, J. A. In "Peptides Polypeptides and Proteins"; Blout, E. R., Bovery, F. A.; Goodman, M.; Lotan, N., Eds; Wiley: New York, 1974; p 320. Snir, J.; Frankel, R. A.; Schellman, J. A. *Biopolymers*, **1975**, *14*, 173.

(13) Singh, R. D.; Keiderling, T. A. *Biopolymers*, **1981**, *20*, 237.

(14) Lal, B. B.; Nafie, L. A. *Biopolymers* **1982**, *21*, 2161.

(15) Dence, J. B. "Steroids and Peptides"; Wiley: New York, 1980.

(16) Harada, N.; Nakaniski, K. *Acc. Chem. Res.* **1972**, *5*, 257.

(17) Hu, E. C.; Holzwarth, G. Abstracts, 167th National Meeting, of the American Chemical Society, Los Angeles, CA, April 1974; No. PHYS 149.

0002-7863/83/1505-6406$01.50/0 © 1983 American Chemical Society

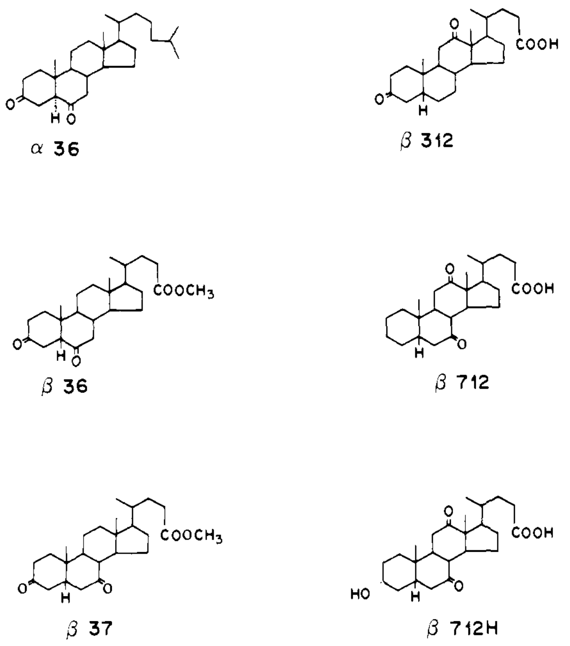


Figure 1. Structure of the various steroids used for the study. α and β refer to the 5 position and the numbers refer to the position of the carbonyls on the steroid skeleton.

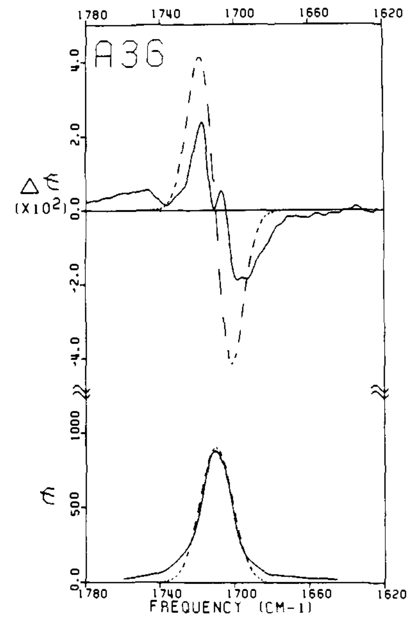


Figure 2. VCD and absorption spectra of α36 0.021 M in CHCl₃. Sample pathlength 0.05 cm, resolution 11 cm⁻¹, and time constant 10 s. Acetone is used for baseline. Four baseline and four sample scans were taken. The theoretically calculated VCD and absorption spectra were plotted (---) using the DCO parameters of Table I. The deflection near zero crossing is noise smoothed out by the lock-in, but the extra band at 1750 cm⁻¹ is real.

Calculational Procedure

From the wide variety of steroid structures known from X-ray crystallography,[18] it seems reasonable to assume that all of the compounds studied will contain six-membered rings in the chair conformation. Fusing of the rings then imposes a definite relative geometry on the two carbonyls. Detailed coordinates of the atoms involved were obtained using the Warshel–Lifson energy minimization technique.[19] Calculations were made for a decalin framework containing two C=O groups in the correct relative positions for each molecule. For β312 and β712, the energy of the complete steroid framework (except the hydrocarbon side chain and acid group) was also minimized. These two calculations gave carbonyl coordinates that were virtually the same as those from the corresponding decalin calculations.

The magnitudes of the dipole moments, $|\mu|$, were obtained by numerically integrating the experimental absorption spectrum over the carbonyl region. For the ester containing compounds, vibrations of the –COOR group somewhat overlap the C=O stretches of interest. In these cases, the dipolar strength was assumed to be equal to the area under a Gaussian function chosen to mimic the lower energy part of the experimental band shape. The dipoles were assumed to lie along the C=O bonds. Tests of the dependence of the calculated VCD on orientation will be discussed in a following section. The DCO formula for rotational strength:

$$R^{\pm} = \mp(\pi\nu/2c)\mathbf{T}_{ab}\cdot(\mu_a \times \mu_b)$$

is also dependent on the interdipolar separation, $\mathbf{T}_{ab}$, and the transition frequency, ν. $\mathbf{T}_{ab}$ was determined from centers of mass of the two carbonyls. In general, ν_0, the single carbonyl frequency, was determined by setting the first moment of the absorption about ν_0 to 0.[20] Sometimes shifting this value slightly gave a better representation of the observed spectrum since the line shape often contained substantial unsymmetrical tails.

To compare calculated $R^{\pm}$ values to experimental VCD, the sign and magnitude of the splitting of the symmetric (ψ^+) and antisymmetric (ψ^-) excited states must be determined. We have assumed that the carbonyls of interest are degenerate and that splitting of the excited state is determined primarily by dipolar coupling energy:[21]

$$V_{ab} = \frac{\mu_a\cdot\mu_b}{|T_{ab}|^3} - \frac{3(\mu_a\cdot\mathbf{T}_{ab})(\mu_b\cdot\mathbf{T}_{ab})}{|T_{ab}|^5}$$

The resulting transition frequencies are then

$$\nu_{\pm} = \nu_0 \pm V_{ab}$$

Using Gaussian line shapes separated by $2V_{ab}$, and of the same half-width as the experimental absorption spectrum, the calculated VCD was plotted as the overlap of the two oppositely signed transitions. Similarly, the calculated absorption spectrum was also plotted using the same linewidths and splitting with individual dipolar strengths of:

$$D^{\pm} = |\mu_a \pm \mu_b|^2$$

To test orientation dependence of the calculated results, a variation of the dipolar direction was introduced by vectorially adding a component in the carbonyl plane. We used a normalized

$$\mu_a^{\pm} = \mu_a \pm c\mu_c$$

where μ_a was along the C=O bond, c was typically 0.1, and μ_c was oriented 120° away, coincident with a C–C bond. To investigate the importance of degeneracy we also treated V_{ab} as a perturbation of two close-lying, nondegenerate states. The resulting energies were than used to plot $\Delta\epsilon$.

Results

The C=O stretching VCD and absorption spectra for α36, β36, β37, β312, β712, and β712H are shown in Figures 2–7, respectively. On each plot the calculated absorption and VCD, determined as described above, is indicated by a dotted line. For all cases except β37 (Figure 4), qualitative agreement between theory and experiment for sign and order of magnitude was obtained.

While the experimental VCD are totally reproducible in sign and general shape, the $\Delta\epsilon$ values varied by up to 25% for duplicated experiments. It can be noted that the small deflections near the zero crossing in α36 and β712 are *not* reproducible but that the extra positive band at 1750 cm⁻¹ in α36 is. Oscillations in the line shape with a ~5-cm⁻¹ period are due to noise smoothed out by the lock-in. The calculated $\Delta\epsilon$ values differ from the exper-

---

(18) Daux, W. L.; Norton, D. A.; "Atlas of Steroid Structure"; IFI/Plenum: New York, 1975; Vol. I.

(19) Lifson, S.; Warshel, A. *J. Chem. Phys.* **1968**, *49*, 5116. Warshel, A.; Karplus, M. *J. Am. Chem. Soc.* **1972**, *94*, 5612. Warshel, A.; Levitt, M. *QCPE* **1974**, *10*, 247.

(20) We set $\int\epsilon(\nu - \nu_0)/\nu\,d\nu = 0$ and solved for ν_0.

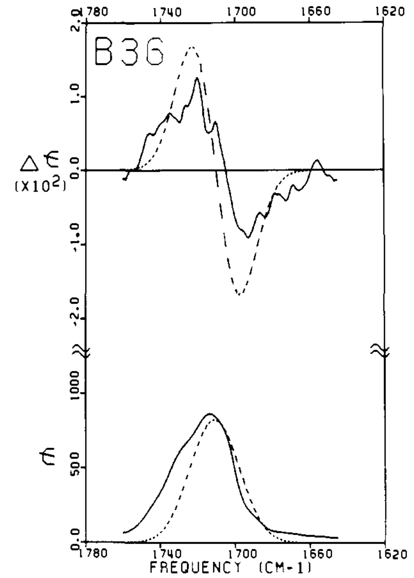


Figure 3. VCD and absorption spectra of β36, 0.0212 M in $CHCl_3$. Sample pathlength 0.035 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone and methyl acetate mixture were used as a baseline. Eight baseline and eight sample scans are averaged. The theoretically calculated VCD and absorption spectra were plotted (- - -) using the DCO parameters of Table I.

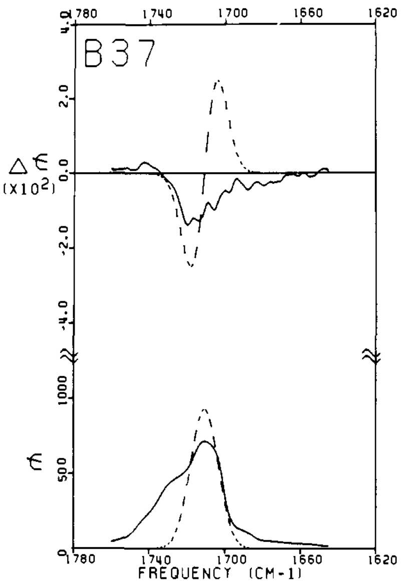


Figure 4. VCD and absorption spectra of β37, 0.0222 M in $CHCl_3$. Sample pathlength 0.025 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone and methyl acetate were used as baseline. Eight baseline and eight sample scans are averaged. Calculated VCD and absorption spectra were plotted (- - -) using the DCO parameters of Table I.

imental ones typically by less than a factor of 2 but at least once (β312) by as much as a factor of 4 (Figure 5). The calculated absorption spectrum best fits experiment for α36, which has no acid or ester groups, while the esters β36 and β37, due to the correction assumed in the previous section, have the worst fit.

A summary of the calculated values for $D^{\pm}$, $R^{\pm}$, V_{ab}, and $\Delta\epsilon$ is presented in Table I along with the experimentally determined ν_0, $|\mu|$, and Δ (linewidth) values and the assumed geometrical parameters. The similarity of the ν, $|\mu|$, and the Δ values serves to reinforce the validity of assuming that the carbonyls are acting as relatively independent, degenerate coupled oscillators. Owing to this consistency, most of the variation in $R^{\pm}$ and V_{ab} values can be related to geometrical differences. In general, because of overlap of the two transitions, both of these parameters are important in determining the sign and magnitudes predicted for $\Delta\epsilon$ (proportional to V_{ab}/Δ and $R^{\pm}$). However, in the cases presented

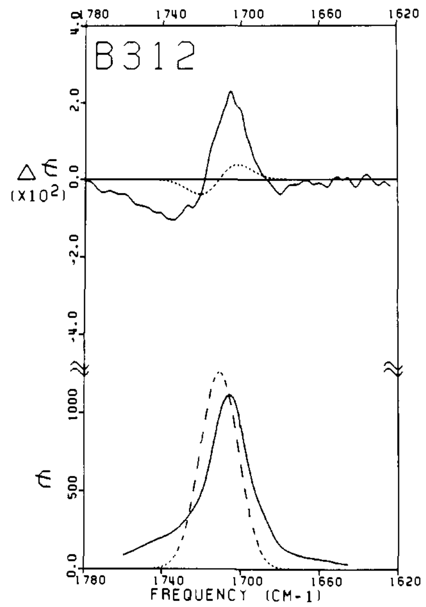


Figure 5. VCD and absorption spectra of β312, 0.021 M in $CHCl_3$. Sample pathlength 0.035 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone was used as baseline. Six baseline and six sample scans are averaged. The theoretically calculated VCD and absorption spectra were plotted (- - -) using the DCO parameters of Table I.

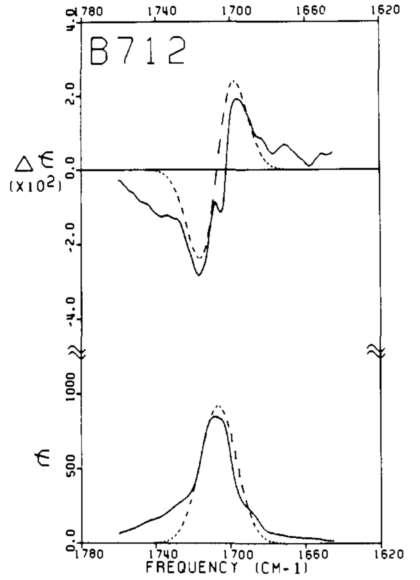


Figure 6. VCD and absorption spectra of β712, 0.026 M in $CHCl_3$. Sample pathlength 0.05 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone was used as a baseline. Four baseline and four sample scans are averaged. The theoretically calculated VCD and absorption spectra were plotted (- - -) using the DCO parameters of Table I and ν_0 moved by 3 cm^{-1} to 1707 cm^{-1}. The deflection near zero crossing is noise smoothed out by the lock-in.

in Table I, all the V_{ab} values are positive and vary by only a factor of 3 in magnitude. Hence the calculated $\Delta\epsilon$ curves primarily reflect the $R^{\pm}$ values.

Additional calculations were made in an effort to evaluate the sensitivity of the calculated VCD to the assumed molecular geometry and, simultaneously, to test the effects of locating the dipole moments along the C=O bond (i.e., assuming that the C=O stretch is not significantly mixed with other internal coordinates). It might be noted that while normal coordinate analysis results for cyclohexanone indicate more than 10% mixing into the C=O stretching mode, these additions all preserve the orientation of the dipolar transition, due to symmetry.[22] Mixing which preserves

---

(21) Tinoco, I. *Radiat. Res.* **1963**, *20*, 133.

Table I. Summary of the DCO Calculation for Six Steroidal Ketones

	experimentally[a] derived parameters			geometrical[b] parameters			DCO calculated values[c]					
steroid	ν_0, cm^{-1}	$\mu \times 10^{19}$ (esu cm)	Δ, cm^{-1}	θ, deg	T_{ab}, Å	ϕ, deg	$D^+ \times 10^{38}$ (esu cm)^2	$D^- \times 10^{38}$ (esu cm)^2	$R \times 10^{42}$ (esu cm)^2	V_{ab}, cm^{-1}	$\Delta\epsilon_{calcd} \times 10^2$	exptl[d] VCD, $\Delta\epsilon_{exptl} \times 10^2$
α36	1710	2.31	11.87	89.3	4.57	63.8	5.39	5.28	3.66	2.27	4.24	2.39 (−1.89)
β36	1710	2.69	17.17	80.3	4.69	16.5	8.45	6.02	1.52	4.76	1.76	1.28 (−0.92)
β37	1711	2.14	10.00	96.1	5.48	322	4.10	5.06	−1.92	1.84	−2.56	−1.50 (0.27)
β312	1711	2.86	13.50	96.7	6.89	352	7.23	9.13	−0.66	1.51	−0.40	−1.07 (2.34)
β712	1710	2.44	13.13	−79.1	5.29	314	4.83	7.08	−2.39	2.45	−2.44	−2.67 (1.94)
β712H	1710	2.66	16.25	−79.1	5.29	314	5.74	8.41	−2.85	2.90	−2.32	−3.44 (2.34)

[a] ν_0 was obtained by setting the first moment of the absorption about ν_0 to zero. μ is the dipole moment. $\mu = (D/2)^{1/2}$, $D = 0.92 \times 10^{-38} \cdot \int \epsilon/\nu \, d\nu$. Δ is the halfwidth at $1/e$ of ϵ_{max}. For esters see text. [b] θ is arc $\cos(\mu_a/|\mu_a| \cdot \mu_b/|\mu_b|)$. ϕ is the dihedral angle between μ_b and μ_a. [c] $\Delta\epsilon_{calcd}$ is calculated assuming Gaussian line shape for absorption.[8a] $\Delta\epsilon^+_{calcd} = 7.48 \times 10^{38} \nu_0 R^+ V_{ab} \pi^{-1/2} \Delta^{-2}$. [d] $\Delta\epsilon_{exptl}$ – value in parentheses is for the lower frequency component.

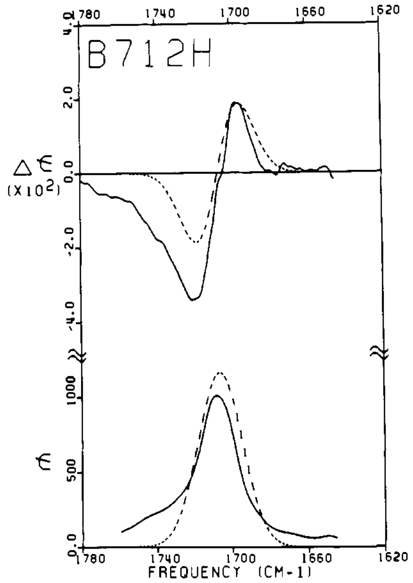


Figure 7. VCD and absorption spectra of β712H, 0.018 M in CHCl$_3$. Sample pathlength 0.035 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone was used as a baseline. Four baseline and four sample scans are averaged. The theoretically calculated VCD and absorption spectra were plotted (- - -) using the DCO parameters of Table I and ν_0 moved 3 cm^{-1} to 1707 cm^{-1}.

the orientation can change the center of mass which may then slightly affect the $\mathbf{T}_{ab}$ values. This should have only a very small effect on the resultant calculated VCD. The mixing we have chosen serves only to distort that direction; hence, we have overestimated the range of orientation error due to such mixing.

$R^{\pm}$, V_{ab}, and $\Delta\epsilon_{calcd}$ were evaluated for all possible combinations of undeviated and deviated dipolar orientations described in the previous section. The results of these calculations are summarized in Table II. For all compounds except β312, the sign and approximate magnitude of $\Delta\epsilon_{calcd}$ were preserved. Most of the variation between orientations occurred in $R^{\pm}$ because the V_{ab} values were relatively stable. For β36, the values did become dramatically smaller in one instance.

In the β312 case, the small $\Delta\epsilon$ value calculated for the minimum energy geometry (Table I) appears to be not small compared to those for alternate geometries but, in fact, is the largest negative value for β312 that we have calculated (Table II). The various β312 geometries in some cases yielded positive values. However, these still remained the smallest $\Delta\epsilon$ calculated for any of the molecules. On the other hand, the β37 calculated results did not show a tendency to sharply decrease, as might have been hoped in view of its observed monosignate VCD, but instead gave a large range of values for $\Delta\epsilon$ (−0.94 to −3 78 × 10^{-2}).

Table II. Geometry Variation and Effect on the DCO Results

dipoles[a]	parameters[b]	α36	β36	β37	β312	β712	β712H[c]
$\mu_a{}^0$, $\mu_b{}^0$	R^+	3.66	1.52	−1.92	−0.66	−2.39	−2.85
	V_{ab}	2.27	4.76	1.84	1.51	2.45	2.90
	$\Delta\epsilon^+_{calcd}$	4.24	1.76	−2.56	−0.40	−2.44	−3.82
$\mu_a{}^+$, $\mu_b{}^0$	R^+	2.82	1.07	−1.33	1.37	−1.67	−1.99
	V_{ab}	1.92	4.62	1.58	1.24	2.18	2.59
	$\Delta\epsilon^+_{calcd}$	2.76	1.20	−1.52	0.67	−1.50	−2.37
$\mu_a{}^-$, $\mu_b{}^0$	R^+	3.78	1.66	−2.64	−0.19	−2.64	−3.14
	V_{ab}	2.16	3.95	1.98	1.48	2.23	2.65
	$\Delta\epsilon^+_{calcd}$	4.18	1.60	−3.76	−0.11	−2.45	−3.82
$\mu_a{}^+$, $\mu_b{}^0$	R^+	2.29	1.29	−1.40	1.40	−1.26	−1.50
	V_{ab}	1.93	4.13	1.54	0.98	2.05	2.44
	$\Delta\epsilon^+_{calcd}$	2.26	1.30	−1.55	0.53	−1.08	−1.68
$\mu_a{}^-$, $\mu_b{}^-$	R^+	3.73	1.08	−1.94	−0.51	−2.7	−3.20
	V_{ab}	1.77	3.54	1.69	1.52	1.88	2.23
	$\Delta\epsilon^+_{calcd}$	3.38	0.94	−2.37	−0.30	−2.10	−3.29
$\mu_a{}^+$, $\mu_b{}^-$	R^+	2.78	0.62	−0.99	1.05	−2.55	−2.09
	V_{ab}	1.52	4.18	1.32	1.30	1.99	2.23
	$\Delta\epsilon^+_{calcd}$	2.16	0.64	−0.94	0.54	−2.12	−2.14
$\mu_a{}^-$, $\mu_b{}^+$	R^+	3.07	0.025	−2.80	0.17	−2.06	−2.45
	V_{ab}	2.12	1.02	1.87	1.14	2.13	2.54
	$\Delta\epsilon^+_{calcd}$	3.32	0.006	−3.78	0.08	−1.83	−2.85
$\mu_a{}^0$, $\mu_b{}^+$	R^+	2.98	1.77	−2.00	0.89	−1.84	−2.19
	V_{ab}	2.25	4.28	1.77	1.16	2.32	2.76
	$\Delta\epsilon^+_{calcd}$	3.43	1.85	−2.55	0.41	−1.78	−2.78
$\mu_a{}^0$, $\mu_b{}^-$	R^+	3.62	0.95	−1.45	0.30	−2.48	−2.94
	V_{ab}	1.83	4.29	1.54	1.56	2.09	2.48
	$\Delta\epsilon^+_{calcd}$	3.39	1.00	−1.61	0.19	−2.15	−3.35
	$\Delta\epsilon_{exptl}$	2.39	1.28	−1.50	−1.07	−2.67	−3.44

[a] $\mu_a{}^0$ and $\mu_b{}^0$ are the dipoles taken along the carbonyl axis. $\mu_a{}^{\pm} = 0.9\,\mu_a{}^0 \pm 0.1\,\mu_c$. [b] Rotational strength (R) in 10^{-42} (esu cm)^2. V_{ab} in cm^{-1}. $\Delta\epsilon_{calcd}$ in 10^{-2} (l mol^{-1} cm^{-1}). [c] Note the values of μ and Δ are different for β712H and β712.

Discussion

In general, the agreement of the DCO calculations with experiment for this set of dicarbonyl steroids is good. However, two of them do give ambiguous results.

The monosignate VCD of the β37 compound obviously does not fit DCO predictions. This is aggravated both by its calculated sigmoidal VCD being both much larger than the experimental noise level and by the stability of the calculated $\Delta\epsilon$ values to modulation of dipolar direction.

---

(22) Fuhrer, H.; Kartha, V. B.; Krueger, P. J.; Mantsch, H. H.; Jones, R. N. *Chem. Rev.* **1972**, *72*, 439.

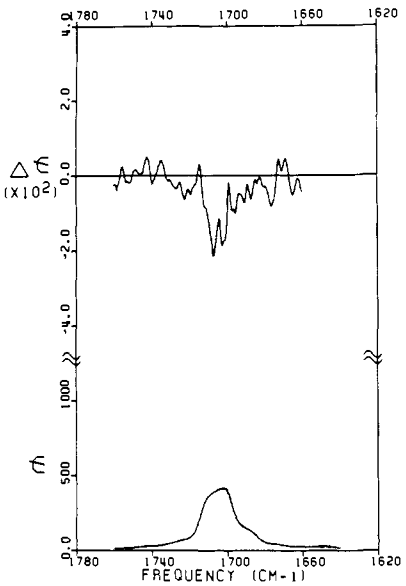


Figure 8. VCD and absorption spectra of 3-oxo-5β-cholanic acid, 0.026 M in $CHCl_3$. Sample pathlength 0.025 cm, resolution 11 cm^{-1}, and time constant 10 s. Acetone was used as baseline. Eight baseline and eight sample scans are averaged. The apparent added noise in this spectrum is due to the use of a different lock-in.

In the second case, the agreement of the β312 experimental and calculated VCD is not maintained over the range of angular variations chosen. Although these were quite large, it might be assumed that the small calculated DCO contribution to the VCD is essentially undetermined and that the apparent agreement in Table I and Figure 5 is fortuitous. Such a conclusion is consistent with the asymmetrical line shape found for β312. It appears that the two C=O stretches may have a largely monosignate VCD while another band of opposite sign overlaps them to higher energy.

Several senarios can be postulated for these difficulties. We will address some of them in this section. First, one might wonder if the DCO model is even operative. One test of this would parallel the distance effect used in the exciton chirality method.[16] Since $\Delta\epsilon$ is proportional to both $R^{\pm}$ and V_{ab} it should vary as $|\mathbf{T}_{ab}|^{-2}$. A plot of the experimental VCD peak-to-peak excursion vs. $R^{+}{\cdot}V_{ab}$ was roughly linear as would be expected for a DCO mechanism. However, the intercept did not pass through zero but was negative, implying that the VCD would be negative for $R^{+}{\cdot}V_{ab}$ equal to zero. This would occur for a single dipole, for dipoles at infinite separation ($V_{ab} = 0$) or for coplanar dipoles ($R = 0$). Such a result was indeed obtained for the VCD of 3-oxo-5β-cholanic acid (Figure 8). We do not have access to a large number of these monocarbonyl compounds to test the generality of this result, but there is no reason to assume that it is general (vide infra). It can further be noted that β37 and β312 have the largest $|\mathbf{T}_{ab}|$ values of the six steroids we have considered.

Nondegeneracy of the oscillators may be a problem in obtaining successful match of theory and experiment. We have calculated the degree of nondegeneracy needed both for the β37 to yield negligible DCO VCD and for the β312 to yield significantly higher VCD. The C=O stretches in these two molecules must be nondegenerate via some other mechanism so that they are split by $\sim$-1.5 cm^{-1} (opposing V_{ab}) and $\sim$6.5 cm^{-1}, respectively, in the absence of dipolar interactions, for the DCO calculations to approximately fit the experimental results. It has been found that while unstrained ketone rings give C=O stretches at 1710 cm^{-1}, the various positions on the steroidal framework can lead to shifts in this value ($\simeq$4 cm^{-1}).[23] Hence, the β312 result appears to be inconsistent with an error in the DCO model due to nondegeneracy, but this could, in principle, explain the β37 result. However, the good agreement for β36, α36, and β712 (which sample the same C=O positions as β37 and β312) implies that these nondegeneracy effects are smaller than needed to explain our results. It can be noted that a nondegeneracy of only 1 cm^{-1} would bring the α36 and β36 experimental and theoretical spectra into optimal agreement.

Since all but one of the compounds are acids and esters, it is reasonable to ask if they or other groups cause distortion of the VCD away from the DCO expected result. From our data we can offer two examples. β36 and α36 differ in the first cyclohexanone ring conformation and also in that the β36 is an ester. The VCD of both are satisfactorily fit by the DCO model which, in addition, nicely predicts the large difference in magnitude due to ring conformation. β36 gives the smallest VCD of any of the compounds; α36 one of the largest (note the scale change in Figure 3 from the others). Significantly, the ester function does not seem to affect the fit.

β712 and β712H both contain acid groups and are identical except for an OH group on the 3 position. They have very similar experimental VCD spectra which are necessarily predicted to be identical by the DCO model. Apparently the C=O groups act relatively independently as assumed in the DCO theory. Hence, while the acid group could perhaps affect carbonyls on the 7 or 12 position and thus distort the β37 and β312 spectra, the β712 results argue against that being a serious problem. The acid form of β37 gave a VCD identical with that of the ester (Figure 4) which further argues against that functional group having a significant effect on the C=O VCD.

It appears that, because of the large number of conformations available to its 4-carbon linkage to the steroid framework, the acid or ester group does not contribute significant VCD in this region. Thus the VCD spectra observed are dominated by that of the local oscillators sought at the outset.

Finally, we must consider the achirality of the oscillators. Clearly, each C=O will give rise to some monosignate VCD, of one sign or the other, as witnessed by our preliminary results (Figure 8). The VCD that is to be compared with the DCO model should be corrected for this effect. Such a correction could hypothetically be made by summing all the component contributions which might be either reinforcing or cancelling. The latter case then would be most adaptable to DCO modelling. A test of this is now not possible but could, in principle, be used to more firmly evaluate the DCO effect. That such monosubstituted VCD's would be additive has not been established, but precedent for such assumption exists in the literature.[24] While in a simple cyclohexanone[25] the C=O VCD is extremely small, it appears that the extensive steroidal framework is a more severe perturbation to the local achirality of the C=O group and can affect VCD dominated by coupling interactions.

Conclusion

This work shows that the DCO model definitely has application to VCD, but the molecules appropriate for study with DCO-VCD must be carefully chosen. Following our earlier work, it is clear that the dipole strengths involved must be very large (for vibrations) and that the oscillators must be highly symmetrical. Small dipolar transitions will not give rise to a significant interaction ($R \sim \mu^2$), and nonsymmetrical oscillators will have a significant, not easily predicted VCD due to local chirality. If the oscillators are not degenerate, they should be distinctly separated in energy and be unambiguously assignable for a modified coupled oscillator calculation to be of use in interpreting the spectrum.

Acknowledgment. This work was supported by grants from the National Science Foundation (CHE81-04997) and the National Institutes of Health (GM 30147). We thank Princeton Applied Research Corp. for a loan of a lock-in amplifier and Professors D. G. Gorenstein and E. A. Gislason for helpful suggestions.

Registry No. α36, 2243-09-6; β36, 1175-04-8; β37, 7753-72-2; β312, 2958-05-6; β712, 21059-35-8; β712H, 517-33-9.

---

(23) Bellamy, L. J. "The Infrared Spectra of Complex Molecules", 3rd ed.; Wiley: New York, 1975; Vol. 2.

(24) Marcott, C.; Blackburn, C. C.; Faulkner, T. R.; Moscowitz, A.; Overend, J. *J. Am. Chem. Soc.* **1978**, *100*, 5262. Marcott, C.; Havel, H.; Overend, J.; Moscowitz, a. *Ibid.* **1978**, *100*, 7088.

(25) Singh, R. D.; Keiderling, T. A. *J. Chem. Phys.* **1981**, *74*, 5347.

J. Am. Chem. Soc. **1983**, *105*, 6411–6416

Optical and Neutron Inelastic Scattering Study of Norbornane: A New Assignment of Vibrational Frequencies

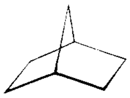
Yvon Brunel,† **Christian Coulombeau,***† **Christiane Coulombeau,**† **Michel Moutin,**† **and Hervé Jobic**‡,⊥

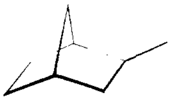
Contribution from LEDSS VI, Domaine Universitaire, BP n° 68, 38402 Saint-Martin-D'Hères Cedex, France, L.A. 332, C.N.R.S. 15, and Institut Laue Langevin, 156 X, 38042 Grenoble Cedex, France. *Received January 24, 1983*

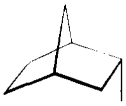
Abstract: We have measured the infrared, Raman, and neutron vibrational spectra of norbornane. The lowest frequency at 172 cm^{-1} has not previously been observed. A normal coordinate analysis based on the Snyder and Schachtschneider valence force field has been carried out. The optical frequencies and neutron intensities calculated with our final force field are in good agreement with the experimental data.

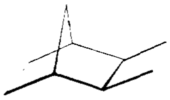
Introduction

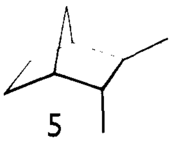
The norbornane molecule (**1**) and some of its derivatives such as the 2-methylnorbornanes (**2**, **3**) and the 2,3-dimethylnorbornanes (**4**, **5**, **6**) constitute an interesting series for studying strain energy effects. The skeletal framework of these molecules is itself a highly strained system, and the additional methyl group interactions present in the substituted compounds vary with their positions (*endo* or *exo*). The additive or specific effects of these interactions can be clarified by a comparative study of these compounds.

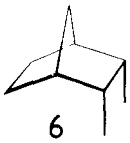

1


2


3


4


5


6

Chemical equilibration performed on the methyl norbornanes[1] and on the dimethyl norbornanes[2] is a first approach toward the correlation of the relative stabilities with molecular structure. The calculation[3] of the free enthalpy differences $\Delta G_T°$ between isomers (**2**, **3**) and (**4**, **5**, **6**) is in good agreement with the experimental values[1,2] and it satisfactorily explains the relative stabilities of these isomers.

The low-frequency vibrations give a large contribution to the enthalpy and entropy terms. They are particularly sensitive to steric interactions which are most important for isomer (**6**).[3]

In a related series of molecules, such as *endo–endo* and *exo–exo* tetracyclo[6,2,1,1,0]dodecanes, Ermer[4] reports the X-ray crystal structure and compares the results with force field calculations. He gives an interpretation of the symmetry of these molecules: the *endo–endo* compound has the C_2 symmetry, without greatly deviating from C_{2v}, while the *exo–exo* has to a good approximation, C_{2v} symmetry. Ermer gives also the calculated lowest frequency value of *endo–endo* and *exo–exo* cyclododecanes (69 and 63 cm^{-1}, respectively) which can be compared with the lowest frequency of norbornane (166 cm^{-1}) and notes that the corresponding normal coordinates involve atomic motions which minimize the hydrogen interactions in space.

In.order to obtain more information on the steric interactions which occur in the norbornane derivatives, we need a complete vibrational analysis of the whole series. The first step is to determine a valence force field for norbornane which may then be transferred to the methyl derivatives.

We have measured the infrared, Raman, and neutron spectra of norbornane and we report in this paper a normal coordinate analysis based on the well-known valence force field of Snyder and Schachtschneider.[5] We have used neutron inelastic spectroscopy (NIS) because, contrary to optical methods, NIS is not bound by selection rules, and because the intensities of the vibrational transitions can be computed through the proton displacements.

Previous Results

The norbornane geometry has been established by electron diffraction[6] (see Figure 1). The strain of the ring system affects the internal coordinates and results in an increase of the CC bond lengths ($C_1C_7 = C_4C_7 = 1.57$ Å,[6a] 1.56 Å [6b]) and in a decrease of the CCC bridge angle ($C_1C_7C_4 = 94°$,[6a] 96°[6b]) Molecular mechanics calculations[7] do not account for the differences between these values and the more usual ones. However, Ermer's calculations[8] have shown a relationship between cross terms such as bond angle force constants and CC bond lengths obtained after minimization of energy.

Two different force fields have been proposed for this molecule; Levin and Harris have published the IR and Raman spectra of norbornane along with a normal coordinate analysis[9] and almost at the same time Meic et al. reported preliminary work using the Snyder and Schachtschneider force constants.[10] However, it appears that the low-frequency vibrations, which have a low intensity in the optical spectra, may not be correctly assigned. For example, the lowest A_2 frequency, which is calculated at 348 cm^{-1} by Levin and Harris,[9] is found at 93 cm^{-1} by Meic et al.[10] (com-

---

† LEDSS VI.

‡ Institut Laue Langevin.

⊥ Present adress: Institut de Recherche sur la Catalyse, 2 Av. Albert Einstein, 69626 Villeurbanne Cedex.

(1) R. J. Ouelette, J. D. Rawn, and S. N. Jreissaty, *J. Am. Chem. Soc.*, **93**, 7117 (1971).

(2) N. A. Belikova, L. I. Kovalenko, M. A. Moskaleva, M. Ordubadu, A. F. Plate, Kh. E. Sterin, and R. S. Yagminas, *Zh. Org. Khim.* **4**, 1363 (1968).

(3) Y. Brunel, C. Coulombeau, and A. Rassat, *Nouv. J. Chim.*, **4**, 663 (1980).

(4) O. Ermer, *Angew, Chem. Int. Ed. Engl.*, **16**, 798 (1977).

(5) R. G. Snyder and J. H. Schachtschneider, *Spectrochim. Acta*, **21**, 169 (1965).

(6) (a) A. Yokozeki and K. Kuchitsu, *Bull. Chem. Soc. Jpn.*, **44**, 2356 (1971); (b) J. F. Chiang, C. F. Wilcox, Jr., and S. H. Bauer, *J. Am. Chem. Soc.*, **90**, 3149 (1968).

(7) (a) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Am. Chem. Soc.*, **92**, 1637 (1970); (b) N. L. Allinger and J. T. Sprague, *J. Am. Chem. Soc.*, **94**, 5734 (1972); (c) E. M. Engler, J. D. Andose, and P. Von R. Schleyer, *J. Am. Chem. Soc.*, **95**, 8005 (1973).

(8) O. Ermer, *Tetrahedron*, **30**, 3103 (1974).

(9) I. W. Levin and W. C. Harris, *Spectrochim, Acta*, **29A**, 1815 (1973).

(10) Z. Meič, M. Randič, and A. Rubcič, *Croat. Chem. Acta*, **46**, 25 (1974).

0002-7863/83/1505-6411$01.50/0 © 1983 American Chemical Society