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CONFORMATIONAL DEPENDENCE OF THE $n \rightarrow \pi^*$ ROTATORY STRENGTH IN DISSYMMETRIC CARBOXYLIC ACID COMPOUNDS[1]

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Abstract—The conformational dependence of the chiroptical properties associated with electronic transitions in α-hydroxy, α-fluoro, α-chloro, and α-mercapto carboxylic acids is examined with a theoretical model in which rotatory strengths are calculated directly from molecular orbitals calculated using INDO and CNDO semi-empirical molecular orbital models, and excited state wave functions constructed in the virtual orbital-configuration interaction approximation. Binding energies, ground state dipole moments, and vertical ionization potentials (calculated according to Koopman's theorem) are calculated, as well as transition energies, dipole strengths, oscillator strengths, rotatory strengths and dissymmetry factors. Special emphasis is placed on correlating the signs of the rotatory strengths calculated for the lowest energy singlet–singlet transitions with conformational isomerism about the C(α)-COOH band of acyclic α-substituted carboxylic acids. The calculated results for *S*-lactic acid are in agreement with and strongly support the empirically based spectra-structure relationships previously proposed for *S*-lactic acid and its derivatives. The calculated results for 2(*S*)-chloropropionic acid do not agree with previously proposed spectra-structure relationships and this finding is discussed. The results obtained for 2(*S*)-mercaptopropionic acid are in partial agreement with experiment and spectra-structure relationships in this case involve some uncertainty.

INTRODUCTION

Considerable attention has been given to the relationship between structure and chiroptical properties in dissymmetric molecular systems containing the carboxyl chromophore.[2] Interest in the structures of these systems includes the electronic origins of the observed spectroscopic properties, intramolecular interactions (as, for example, between the carboxylate moiety and other groups in the molecules), and molecular stereochemistry (absolute configuration and conformational isomerism). Special emphasis has been placed on the relationship between the sign and relative magnitude of the Cotton effect (CE) associated with the lowest lying singlet–singlet electronic transition ($n \rightarrow \pi^*$) of the carboxyl group and specific conformational or other stereochemical features of simple carboxylic acids containing an asymmetrically substituted α-carbon atom. Sector rules have been proposed for the $n \rightarrow \pi^*$ CE in simple carboxylic acids and these semi-empirically based rules have been found useful for correlating the sign of experimentally determined CE with absolute configuration at the asymmetric α-carbon and with conformational equilibria about the C_α-COOH bond. The sector rules applied to $n \rightarrow \pi^*$ carboxylic acid transitions were derived directly from similar sector rules developed for chiral lactone systems.

The empirical and semi-empirical spectra-structure relationships developed for chiral carboxylic acid derivatives have been useful for providing systematic interpretations of the chiroptical properties associated with the carboxyl $n \rightarrow \pi^*$ transition. The proposed sector rules are based, however, on qualitative or semiquantitative representations of the electronic structure and spectroscopic states of the carboxyl chromophore. This is made necessary by the lack of detailed information on the electronic structure and states of the $-COO^-$ group in complex systems. The theoretical underpinnings of the "carboxyl sector rule" can be evaluated only after the electronic states of the carboxyl group have been thoroughly characterized and the nature of the interactions between the carboxyl moiety and the non-carboxyl (vicinal) groups has been described.

With the exception of our own work[3] and that of two other groups on aliphatic α-amino acids,[4,5] purely theoretical calculations on the chiroptical properties of dissymmetric carboxylic acid derivatives have not been reported. In the present paper, we report results of calculations on the electronic structure and spectra of conformational isomers of *S*-lactic acid, 2(*S*)-chloropropionic acid, 2(*S*)-fluoropropionic acid and 2(*S*)-mercaptopropionic acid. Special emphasis is placed on the chiroptical properties associated with the lowest energy singlet–singlet transitions in these systems and the relationship between these properties and stereochemical variables. The calculations are based on the INDO-MO (intermediate neglect of differential overlap-molecular orbital) and CNDO-MO (complete neglect of differential overlap-molecular orbital) models for the ground state valence-shell electronic structure of the molecules, and the virtual orbital-configuration interaction method is employed in constructing electronic excited states. The primary objective of this study is to provide a theoretical basis for interpreting the chiroptical spectra of simple α-hydroxy, α-halo and α-mercapto carboxylic acids (and their derivatives) in terms of specific stereochemical and electronic structural features.

The approximate nature of the calculations performed in this study do not permit using the results to "test" the sector rules developed and proposed on purely empirical or semi-empirical grounds. The calculations do, however, provide an alternative theoretical basis on which to interpret the chiroptical properties associated with the lowest energy electronic transitions in simple dissymmetric carboxylic acid compounds. Semi-empirical molecular orbital models (such as the one employed here) have been used extensively in recent years to calculate the chiroptical properties of dissymmetric molecular systems.[3,6,7]

METHODS OF CALCULATION

The ground state electronic wave functions for the *S*-lactic acid and 2(*S*)-fluoropropionic acid structures are calculated on the INDO-MO model of Pople *et al.*,[8] and

the ground state electronic wave functions for the 2(*S*)-mercaptopropionic acid and 2(*S*)-chloropropionic acid structures are calculated using the CNDO-MO model.[8] "Standard" parameters[8] are employed in both the INDO and CNDO calculations and 3d orbitals are included in the atomic orbital basis sets for the structures which contain S or Cl atoms. Excited states are constructed in the virtual orbital-configurations interaction (CI) approximation and only singly-excited configurations are admitted into the CI basis set.

Prior to calculating electric and magnetic dipole transition integrals between the ground and excited states, the molecular orbitals obtained from the INDO (or CNDO) calculations are renormalized to include overlap. That is, the eigenvector matrix $\tilde{C}_\lambda$ is subjected to the transformation, $\tilde{C}_\chi = \tilde{S}_\chi^{-1/2}\tilde{C}_\lambda$, where $\tilde{S}_\chi$ is the overlap matrix over the Slater atomic orbital basis set $\tilde{\chi}$. The molecular orbitals are then expressed as,

$$\tilde{\phi} = \tilde{C}_\lambda\tilde{\lambda} = \tilde{C}_\chi\tilde{\chi} \tag{1}$$

where the functions $\tilde{\lambda}$ comprise the orthogonal INDO (or CNDO) basis set. All electric and magnetic dipole transition integrals are calculated in the Slater basis $\tilde{\chi}$. Additionally, all one-center and two-center terms are included in our calculations of the transition integrals.

The optical properties we calculate and report are: (a) dipole strength,

$$D_{ij} = |\langle\psi_i|\hat{\mu}|\psi_j\rangle|^2. \tag{2}$$

(b) oscillator strength,

$$f_{ij} = (4\pi\nu_{ij}m/3he^2)D_{ij} \tag{3}$$

where $\nu_{ij} = (E_i - E_j)/h$; (c) reduced rotatory strength,

$$[R_{ij}] = (100/\beta D)\,\mathrm{Im}\,\langle\psi_i|\hat{\mu}|\psi_j\rangle\cdot\langle\psi_j|\hat{m}|\psi_i\rangle \tag{4}$$

where β is the Bohr magneton, D is the Debye unit, $\hat{\mu}$ is the electric dipole operator, and $\hat{m}$ is the magnetic dipole operator; and, (d) dissymmetry factor,

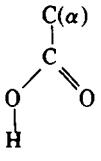
$$g_{ij} = 4R_{ij}/D_{ij}. \tag{5}$$

The electric dipole transition integrals are calculated in the dipole velocity formalism and ground state electric dipole moments are calculated according to the method outlined by Pople.[8]

STRUCTURES

S-*Lactic acid*

Six conformational isomers of unionized *S*-lactic acid were studied. In each of these structures the C(α) atom and the carboxyl group proton were arranged in a trans configuration.



trans arrangement of C(α) and H(O)

The conformational prarameters which were varied among the six isomers are rotation about the C(α)-COOH bond and rotation about the C(α)-OH bond. With respect to the latter parameter, we chose just two orientations of the OH group: (a) the O–H bond directed away from the carboxyl group; and, (b) the O–H bond directed towards the carboxyl group. Three rotameric isomers about C(α)-COOH are represented among the six structures: L_1, in which the α-OH group lies in the plane of the –C(α)COOH group; L_2, in which the α-H atom lies in the plane of –C(α)COOH; and, L_3, in which the carbon atom of the α-CH_3 group lies in the plane of the –C(α)COOH group. These rotameric isomers are depicted in Fig. 1. Note that the α-substituent lying in the plane defined by the –C(α)COOH group eclipses the carbonyl oxygen atom in each of the structures L_1, L_2 and L_3. We shall refer to the six *S*-lactic structures as: L_1a, L_2a and L_3a in which the O–H bond is directed *away* from the carboxyl group; and, L_1b, L_2b and L_3b in which the O–H bond is directed *towards* the carboxyl group.

2(S)-*Mercaptopropionic acid*

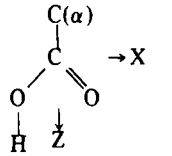
Three conformational isomers of 2(*S*)-mercaptopropionic acid were studied. In each of these structures the C(α) atom and the carboxyl group proton were arranged in a trans configuration and the S–H bond of the α-SH substituent was directed towards the carboxyl group. The three isomers were generated by rotation about the C(α)-COOH bond and are named as follows: M_1b, in which the SH substituent lies in the plane of the –C(α)COOH group and S–H is directed towards the carboxyl group; M_2b, in which the α-H atom lies in the –C(α)COOH plane; and, M_3b, in which the carbon atom of the α-CH_3 group lies in the same plane as –C(α)COOH. The carbonyl oxygen atom is eclipsed by an α-substituent in each of these three structures.

2(S)-*Fluoro- and* 2(S)-*chloropropionic acid*

Three conformational isomers of each of these two compounds were studied. These isomers are rotamers about the C(α)-COOH bond and correspond to the structures depicted in Fig. 1. In each structure the carbonyl oxygen atom is eclipsed by an α-substituent and the C(α) atom and the carboxyl group proton are trans to each other. We shall refer to the 2(*S*)-fluoropropionic acid structures as F_1, F_2 and F_3, and to the 2(*S*)-chloropropionic acid structures as C_1, C_2 and C_3.

Coordinate system

A common coordinate system is employed for all 15 structures studied. The origin is located at the C(α) atom and the z-axis is coincident with the C(α)-COOH bond.



Y is up.

RESULTS

The ground state electric dipole moments, binding energies, and first two ionization potentials calculated for each of the 15 structures are listed in Table 1. The optical properties calculated for *S*-lactic acid and 2(*S*)-fluoropropionic acid isomers are displayed in Table 2. In Table 3, the components of the electric and magnetic dipole transition integrals are presented for the $n \rightarrow \pi^*$ transition in the *S*-lactic acid and 2(*S*)-fluoropropionic

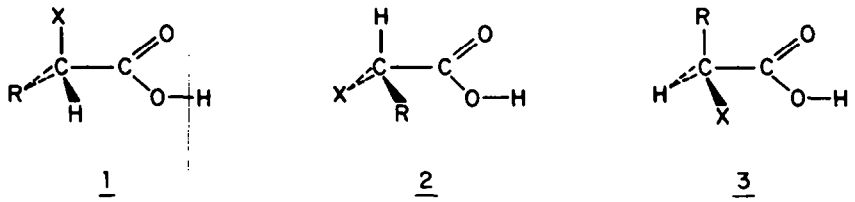


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Fig. 1. Rotameric isomers of α-X alkyl carboxylic acids (X = OH, F, Cl, SH, and R = CH_3 in the present study).

Table 1. Calculated dipole moments,[a] binding energies and vertical ionization potentials[b]

Structure	Dipole moment	Binding energy (au)	IP_2 (au)	IP_2 (au)
L_1a	3·54	−4·1426	0·433	0·477
L_1b	2·62	−4·1467	0·445	0·477
L_2a	2·41	−4·0173	0·407	0·478
L_2b	2·33	−4·1352	0·431	0·486
L_3a	2·21	−4·0085	1·415	0·473
L_3b	2·19	−4·1339	0·435	0·488
F_1	3·42	−3·9057	0·448	0·504
F_2	2·19	−3·9445	0·455	0·514
F_3	1·84	−3·9376	0·466	0·515
C_1	3·42	−4·0734	0·491	0·519
C_2	2·27	−4·0777	0·486	0·523
C_3	2·21	−4·0790	0·490	0·522
M_1b	3·51	−4·2314	0·453	0·489
M_2b	2·07	−4·2355	0·463	0·471
M_3b	2·12	−4·2340	0·462	0·478

[a] In Debye units.
[b] Calculated according to Koopman's theorem.

Table 2. Optical properties calculated for the lowest singlet–singlet transition (n→π*) in the *S*-lactic acid and 2(*S*)-fluoropropionic acid structures

Structure	ΔE (eV)	λ (nm)	f	D (Debye)	[R]	|g|
L_1a	5·64	220	0·0050	0·237	3·90	0·0061
L_1b	5·71	217	0·0103	0·475	2·89	0·0022
L_2a	5·50	225	0·0075	0·358	3·77	0·0039
L_2b	5·30	234	0·0014	0·095	5·21	0·0219
L_3a	5·30	234	0·0111	0·540	−11·19	0·0077
L_3b	5·20	239	0·0034	0·238	−7·82	0·0131
F_1	5·42	229	0·0058	0·306	4·82	0·0063
F_2	5·45	227	0·0059	0·308	−3·85	0·0050
F_3	5·41	229	0·0082	0·431	−5·39	0·0050

Table 3. Components of the electric and magnetic dipole transition integrals for the n→π* transition

	Electric[a]			Magnetic[b]		
Structure	X	Y	Z	X	Y	Z
L_1a	0	0·038	−0·008	−0·370	0·011	−0·329
L_1b	0·002	−0·057	0·005	0·412	−0·002	0·247
L_2a	0·005	−0·046	−0·012	−0·439	−0·040	−0·293
L_2b	0·001	−0·015	0·011	0·429	−0·011	0·318
L_3a	0·005	0·045	−0·035	0·534	−0·069	0·254
L_3b	0·008	0·030	0·005	−0·431	−0·043	−0·257
F_1	−0·001	−0·039	−0·015	−0·704	−0·014	−0·190
F_2	0·004	−0·042	0·001	−0·665	−0·002	−0·216
F_3	0·002	0·046	−0·018	0·682	−0·024	0·226

[a] Dipole velocity integrals, $\langle\psi_o|\partial/\partial q|\psi_n\rangle$, expressed in atomic units. q = x, y or z.
[b] $(e/2mc)\langle\psi_o|L_q|\psi_n\rangle$ in Bohr magneton units. $L_q = L_x$, L_y or L_z.

acid structures. The optical properties computed for the three lowest energy transitions of the 2(*S*)-chloro- and 2(*S*)-mercaptopropionic acid structures are given in Table 4.

The highest occupied orbital in the structures L_1b, L_2b, L_3b, F_1, F_2 and F_3 is almost entirely localized on the carbonyl group with its largest amplitude on the carbonyl oxygen atom. It can be classified as a carbonyl n (nonbonding) orbital. The lowest unoccupied orbital calculated for these structures is also localized on the

Table 4. Optical properties calculated for the three lowest singlet–singlet transitions in 2(*S*)-chloro- and 2(*S*)-mercaptopropionic acid

Structure	ΔE(eV)	f	D(Debye)	[R]	|g|
C_1	4·82	0·0817	4·500	1·44	0·0001
	4·84	0·0904	4·944	−0·04	0
	6·35	0·0134	0·558	−7·92	0·0053
C_2	4·67	0·1032	5·832	8·92	0·0006
	4·76	0·0877	4·854	−3·35	0·0004
	6·33	0·0256	1·068	−17·51	0·0061
C_3	4·74	0·1039	5·881	−8·80	0·0009
	4·84	0·0966	5·289	2·55	0·0002
	6·15	0·0199	0·839	13·98	0·0062
M_1b	3·46	0·0821	6·261	−20·69	0·0012
	3·99	0·0025	0·172	4·49	0·0099
	6·98	0·0112	0·423	7·16	0·0063
M_2b	3·46	0·0763	5·816	−18·50	0·0012
	3·89	0·0072	0·489	12·61	0·0096
	7·05	0·0034	0·126	4·82	0·0142
M_3b	3·46	0·0768	5·860	−16·93	0·0011
	3·88	0·0067	0·454	0·75	0·0006
	7·08	0·0039	0·146	0·24	0·0006

carboxyl group and is best described as a carboxyl group π^* orbital.

In structures L_1a, L_2a and L_3a, the highest occupied orbital is again principally localized on the carboxyl group, but in this case the 2p atomic orbitals on the α-OH group also contribute. The lowest unoccupied orbital of L_1a, L_2a and L_3a is principally carboxyl π^*, but it too reflects some α-OH 2p orbital character.

The lowest singlet excited state of structures L_1a, L_2b, L_2a, L_2b, L_3a, L_3b, F_1, F_2 and F_3 can be characterized as essentially a carboxyl-group-localized $n\pi^*$ state, keeping in mind that for structures L_1a, L_2a and L_3a the n and π^* orbitals also include some α-OH group character.

The two lowest energy transitions in the mercapto-substituted structures are $n\rightarrow\sigma^*$ type excitations localized on the –SH group. The third transition in these structures is an $n\rightarrow\pi^*$ carboxyl group transition.

The lowest energy transition in the α-chloro structures is localized on the Cl atom. The second transition, which is nearly degenerate with the first, involves considerable Cl→COOH charge-transfer. The third transition is primarily localized on the carboxyl group and may be classified as $n\rightarrow\pi^*$.

DISCUSSION

The results presented in Table 2 suggest that the sign of the $n\rightarrow\pi^*$ CE in lactic acid may be related to conformational preference with respect to rotation about the C(α)-COOH bond. Rotamers 1 and 2 of Fig. 1 will give a positive $n\rightarrow\pi^*$ CE for *S*-lactic acid, whereas rotamer 3 will yield a negative CE. The calculated results also predict that the relative λ_{max} values for the $n\rightarrow\pi^*$ transition in rotamers 1, 2 and 3 will fall in the order: $\lambda_{max}(1) < \lambda_{max}(2) < \lambda_{max}(3)$. That is, in going from rotamer 1 to 2 to 3, λ_{max} is progressively red-shifted. These results offer support for the hypothesis[2d] that the predominant CE centered at ~210 nm in α-hydroxy acids is due to a conformational isomer of type 1, and that the longer wavelength and oppositely signed CE (~240 nm) observed only under certain solvent and pH conditions is attributable to a conformational isomer of type 3. Listowsky, Avigad and Englard[2d] reasoned that isomers of type 2 were the least stable and did not contribute significantly to the observed CD.

For *S*-lactic acid in 95% ethanol, Craig and Pereira[2h] reported the following CD data: $\lambda_{max} = 244$ nm, $[\theta]_{max} = -14{\cdot}6$; $\lambda_{max} = 210$ nm, $[\theta]_{max} = 2727$. For *S*-lactic acid in water at pH 1, these same authors reported: $\lambda_{max} = 246{\cdot}5$ nm, $[\theta]_{max} = -17{\cdot}4$; $\lambda_{max} = 212$ nm, $[\theta]_{max} = 2157$. They found only one CD band at $\lambda > 200$ nm for *S*-lactic acid in water at pH 9; this band was centered at 214 nm with a molar ellipticity of 744. Barth *et al.*[2f] studied the temperature dependence of the CD spectra of several lactic acid derivatives and found that the long wavelength band (~240 nm) decreased in intensity with decreasing temperature, whereas the 210–215 nm CD band increased in intensity with decreasing temperature. These workers concluded that both CD bands at $\lambda > 200$ nm could be assigned to the carboxyl group $n\rightarrow\pi^*$ transition. They attributed the presence of two bands either to specific solvation effects or to conformational equilibria between conformers with different chiroptical properties.

Anand and Hargreaves[2g] also studied the CD of *S*-lactic acid in a number of solvents and assigned the weak, lower energy CD band to an $n\rightarrow\pi^*$ carboxyl transition and the more intense, higher energy band ((~210–215 nm) to a $\pi\rightarrow\pi^*$ carboxyl transition. These assignments are in direct conflict with the more conventional view that the CE associated with the 210 nm absorption band of carboxylic acids and their ester derivatives is of $n\rightarrow\pi^*$ origin.

The calculated results listed in Table 2 for conformational isomers of *S*-lactic acid support the view that the higher energy positive CE can be attributed to a $n\rightarrow\pi^*$ transition in isomers L_3a and/or L_3b. That is, these calculations support the suggestions made previously by Listowsky, Avigad and Englard[2d] and by Barth *et al.*[2f] The binding energies calculated for the six *S*-lactic acid isomers (see Table 1) also support the view that rotamer 1 should be energetically favored over both rotamer 2 and rotamer 3. This result is consistent with the CD data obtained from temperature-dependent studies.[2f] A decrease in temperature should decrease the populations of rotamers 2 and 3 and increase the population of rotamer 1, resulting in a decrease in the negative CE at ~240 nm and an increase in the positive CE at ~210–215 nm.

We also note that the computed dipole moments for structures L_1a and L_1b are larger than for structures L_2a, L_2b, L_3a and L_3b. This suggests that rotamer 1 will interact more strongly with polar solvents than rotamers 2 and 3, and will be energetically favored through solute–solvent interactions. In solvents of lower polarity, the populations of rotamers 2 and 3 should increase. The experimentally determined CD data on *S*-lactic acid and its derivatives generally show that the intensity of the 210–215 nm band increases and the intensity of the 240 nm band decreases as solvent polarity is increased. This experimental result is in agreement with the view that rotamer 1 is most favored in polar solvents.

In general, our calculated results are in remarkable agreement with the empirically and semi-empirically based conclusions arrived at previously by several workers[2d,2f] concerning spectra-structure relationships for lactic acid and lactic acid derivatives. The CD of 2(*S*)-fluoropropionic acid has not been reported.

The results given in Table 3 show that the carboxyl $n\rightarrow\pi^*$ transition in lactic acid and in 2-fluoropropionic acid is strongly magnetic dipole allowed with polarization in the xz-plane (the plane of the C(α)COOH group).

The CD, ORD, and absorption spectra of 17 α-chloro and α-bromo alkyl carboxylic acids were measured and

reported by Gaffield and Galetto.[2e] The alkyl groups were varied from methyl(2-chloropropionic acid) to t-butyl and both the solvent-dependence and temperature-dependence of the CD for several of the compounds were investigated. For the compounds of *S* absolute configuration, two CD bands were found in the region $\lambda > 200$ nm. One band is positive with a maximum at 195–222 nm and the second band is negative with a maximum at 233–270 nm. The CD spectra were interpreted by Gaffield and Galetto on the basis of conformational equilibria and they concluded that the preferred conformation for all the α-halo acids studied is the C(α)-COOH rotamer which has the halogen atom eclipsed with the carbonyl, $\rangle C{=}O$, group. Gaffield and Galetto assumed that both CD bands at $\lambda > 200$ nm could be assigned to a carboxyl group n→π* transition. They proposed that a rotamer of type 1 (see Fig. 1) is responsible for the higher energy band and that a rotamer of type 3 gives rise to the lower energy band. This relationship between conformation and CD in α-halo acids is similar to that proposed by Listowsky *et al.*[2d] for α-hydroxy acids.

Our calculated results for 2(*S*)-chloropropionic acid (Tables 1 and 4) appear to be in distinct disagreement with the assignments and spectra-structure relationships proposed by Gaffield and Galetto. Based on our calculated results, the lower energy CD band would be attributed to two nearly degenerate transitions, one localized on the Cl atom and one involving Cl→COOH charge-transfer. The higher energy CD band at ~200 nm would be assigned to the carboxyl n→π* transition. Furthermore, structure C_3 (rotamer 3) is predicted to be energetically favored over structures C_1 and C_2. If, in fact, structure C_3 is the predominant structure in solution then the calculated rotatory strengths for C_3 agree with the experimentally determined CD spectrum which shows a negative CE centered at ~235 nm and a positive CE centered at ~200 nm.

These remarks must be considered with some caution, however, in view of the limitations of our theoretical model for calculating the electronic properties of molecules containing second row atoms such as Cl. There is little experimental evidence that a Cl atom substituted nearby to a carboxyl or carbonyl moiety should result in two low lying excited states which are either Cl→COOH charge-transfer in nature or largely localized on the Cl atom, and which lie lower in energy than does the first carboxyl nπ* state. These states certainly should exist and might possibly be observable in the CD and absorption spectra measured in nonpolar solvents. However, it is questionable whether they would lie below the carboxyl nπ* state. If we neglect our two lowest energy calculated transitions, accept the assignments of Gaffield and Galetto, and compare our calculated results for the carboxyl n→π* transition with their proposals, we again find disagreement. Gaffield and Galetto proposed that the n→π* transition in the rotamer of type 1 (see Fig. 1) is responsible for the positive CE observed in the 195–222 nm region, and that the n→π* transition in a rotamer of type 3 gives rise to the negative CE appearing in the 233–270 nm region. Furthermore, they concluded from their temperature dependence studies that rotamer 1 is the most stable of the C(α)-COOH rotameric isomers. Our calculations yield a negative CE for the n→π* transition of rotamer 1, a positive CE for the n→π* transition in rotamer 3, and a slightly more favorable binding energy for rotamer 3 vs rotamer 1. We emphasize the possible difficulties in our theoretical model for calculating the spectroscopic properties of molecules containing second row atoms such as Cl, but we also believe that the previous proposals concerning spectra(CD)-structure relationships for α-halo acids must be considered with some reservation until further empirical data or more refined theoretical analyses are available.

The ORD and CD of 2(*R*)-mercaptopropionic acid has been reported by Scopes, Thomas and Rahman.[2j] In hexane, the CD spectrum of this compound shows the following features: positive maximum at 240 nm ($\Delta\epsilon$ = 2·10), shoulder at 220 nm ($\Delta\epsilon$ = 1·48), and a negative maximum at 198 nm ($\Delta\epsilon$ = −2·26). The absorption spectrum exhibits an inflection at 235 nm (ϵ = 210) and a maximum at 206 nm (ϵ = 700). For the *S* enantiomer of 2-mercaptopropionic acid one should find an intense negative CE around 240 nm, a weaker negative CE near 220 nm, and an intense positive CE near 205 nm.

Our calculations predict a negative CE for the lowest energy transition (sulfur localized n→σ*) of 2(*S*)-mecaptopropionic acid in each of the three isomeric forms, M_1b, M_2b and M_3b. The second (sulfur localized n→σ*) and third (carboxyl n→π*) transitions are predicted to give positive CE's in each of the three isomeric forms. The transition energies calculated for the sulfur localized n→σ* excitations are lower than the experimental results show them to be and the oscillator strengths for these transitions are calculated to be larger than can be supported by the experimental results.

SUMMARY

Employing the INDO and CNDO semi-empirical molecular orbital models we have calculated the electronic rotatory strengths of transitions lying at $\lambda > 195$ nm for a number of acyclic α-substituted carboxylic acids. We considered only those isomeric forms of these compounds which have been implicated in establishing spectra-structure relationships for chiral α-substituted carboxylic acids. In most previous studies on the chiroptical properties of such systems, it has been assumed that the most stable rotamers about the C(α)-COOH bond are those in which one of the α-substituents lies in the plane formed by the C(α)COOH group and eclipses the carbonyl group. This assumption appears to be supported by a wide variety of structural studies and by the argument that rotation about a $C(sp^3)$–$C(sp^2)$ bond favors a conformation in which the $C(sp^3)$ substituent lies in the nodal plane of the π system formed by $C(sp^2)$. Spectra (CD)-structure relationships proposed for acyclic α-substituted carboxylic acids generally have been based on assumptions about rotamer populations or conformational equilibria involving the rotameric forms displayed in Fig. 1. A number of empirical and semiempirical rules have been developed relating the sign of the carboxyl group n→π* CE to various structural features and to conformational equilibria of these systems in solution at different temperatures and with different solvents.

The calculated results presented here are in agreement with and provide strong support for several of the extant spectra-structure relationships proposed for α-hydroxy carboxylic acids. In particular, they support the conclusions on conformational equilibria and stereochemical relationships presented in the very thorough study reported by Listowsky, Avigad and Englard.[2d] The calculated results for α-chloro substituted systems are less definitive and appear to be in disagreement with the

conclusions arrived at by Gaffield and Galetto.[2e] However, the theoretical model is expected to be less reliable for calculations involving second row atoms such as Cl, and these results must be considered with some circumspection. The same qualifying statement must also be made for the calculations performed on the 2-mercaptopropionic acid system, although in this case the sign calculated for the lowest energy CE appears to be in agreement with experiment.

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