CHIROPTICAL PROPERTIES OF α-SUBSTITUTED SUCCINIC ACIDS

CONFORMATION AND ABSOLUTE CONFIGURATION[1]

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Abstract—The effect of conformational preference on the chiroptical properties of α-substituted succinic acids and esters 2 has been investigated using variable-temperature CD in solvents of different polarity. All available evidence indicates that when R' in 2 is alkyl or halogen, the preferred conformation is 1e with the –CH₂COOR group eclipsed by the C=O bond, while when R' in 2 is hydroxy, methoxy or amino, the major conformer is 1d in which the heteroatom is eclipsed by the C=O bond. In both cases, conformation 1f appears to be the least favored, mainly on steric grounds. The results when R' = chloro or bromo do not support previously proposed conclusions and an alternative explanation is advanced. In the resultant octant projection (Fig. 2) it is shown that the sign of the Cotton effect for 1 will be determined by the position of the groups X and Y in the back octants, and since one of these is always H in the two favored conformations, the sign is actually determined by the position of the other group. This octant projection predicts successfully the sign of the ellipticity of the n → π* transition for any α-substituted succinic acid or ester with the appropriate substituent R', and appears to apply also to simple alkanoic acids and esters with the same substituents.

The electronic transitions of carboxylic acids or esters in the near UV region have received much attention during the last ten years. However, although a considerable amount of experimental data relating to the carboxyl chromophore has been generated, the development of a successful theoretical treatment of this subject is far behind that of the CO transitions.[3/4] The simple CO group exhibits a well known low intensity, low energy absorption near 290 nm, due to an n → π* transition. It is generally believed that when –OR is attached to the CO group, interaction of the nonbonding electrons on the ether oxygen with the π-orbitals of the CO group raises the energy of the antibonding π-orbital and splits the bonding π-orbital into two new orbitals, π_1 and π_2, the latter being essentially a nonbonding orbital located mainly on the ether oxygen. An approximate energy diagram for the carboxyl chromophore is presented in Fig. 1.[3] The two transitions of lowest energy then belong to $n - \pi_3^*$ and $\pi_2 - \pi_3^*$.

From the energy diagram, the n → π* transition of the carboxyl group is predicted to appear at shorter wavelength than the corresponding ketone transition. In fact, a weak absorption band is observed to occur near 210 nm which fulfills all the criteria used[3] in the identification of n → π* transitions: (a) low intensity (since it is symmetry forbidden), (b) "blue shift" of the maximum caused by electron-supplying substituents attached directly to the π-system, (c) "blue shift" of the maximum with increasing polarity of the medium, and (d) obliteration of vibrational fine structure on changing from nonpolar to polar media.

In general, CD and UV show the same or similar wavelengths of absorption maxima in the spectrum. For optically active aliphatic carboxylic acids or esters, a Cotton effect is always observed near 210 nm.[5] However, recent CD studies of α-hydroxy acids of S-(+)-configuration have shown[6-9] two optically active bands in the 200–250 nm region: the normal positive 210 nm band and an abnormal negative 245 nm band. Similar findings[9,10] were also extended to the α-amino acids, i.e. the S-(+)-acid has a small CD of opposite sign at higher wavelength which disappears on protonation of the amino group. A possible explanation for the occurrence of such
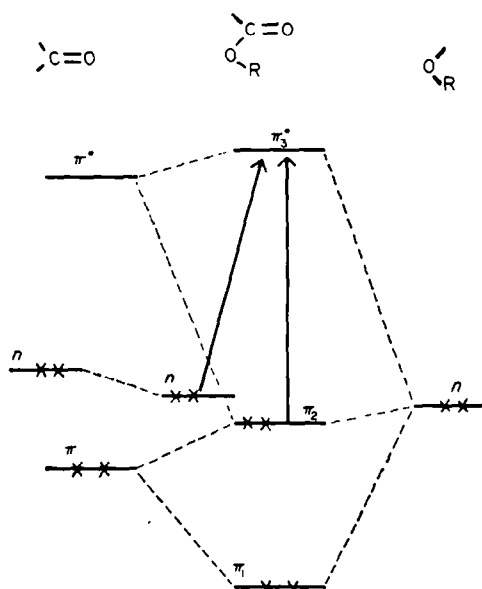

Fig. 1. Energy level scheme for the ester carbonyl system.[3]

a phenomenon was the existence of conformational isomerism as shown by low temperature measurements,[7] leading to the conclusion that both bands belong to the same n → π* transition of the carboxyl group.

An empirical treatment of the optically active carboxyl transition has led to the development of the so-called "lactone rule"[11] for the correlation of chiroptical behavior and configuration of lactones. However, due to the complex nature of the carboxyl transition, the boundaries used in this rule for Cotton effect sign assignment are very difficult to define, and the usefulness of the "lactone rule" is thereby seriously diminished. From Fig. 1, it can be seen that, for the carboxyl n → π* transition, the electrons involved are mainly localized on the carbonyl oxygen, therefore *the ground state symmetry of this transition should be the same as that of the ketone chromophore.* On this basis, the ketone octant rule[12] should also be applicable to optically active α-substituted acids or esters. If the octant rule is applied to an α-substituted acid (1, R=H), the sign assignment of the back octant, defined as in an α-substituted cyclohexanone,[12] would be as shown in Fig. 2. Since octant rule data are based mostly on α-halo and α-methyl substituent, we decided to examine, initially, the chiroptical behavior of some α-methyl and α-halo substituted acids and then to extend this to the study of acids with other α-substituents.
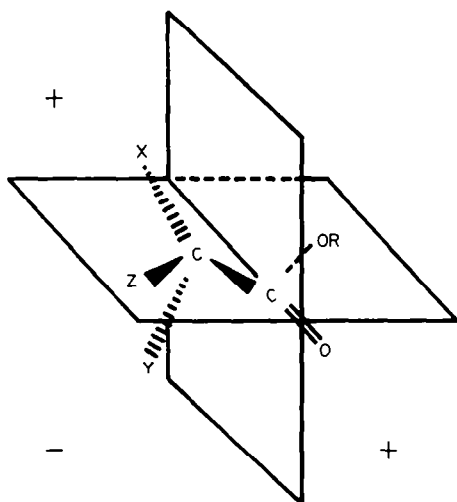

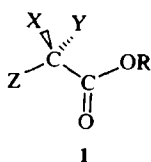Fig. 2. Sign assignment for back octants of an α-substituted acid or ester 1.

α-Alkyl succinic acids and esters

The simplest α-Me substituted optically active acid that may be used for CD study would be α-methylbutyric acid (of which 1, X=H, Y=Me, Z=Et is one conformer). However, the very similar nature of the α-alkyl groups, and the resulting conformational equilibrium, would be expected to result in a low intensity CD band.[13] For this reason, we chose to investigate the corresponding α-alkyl

succinic acids (1, R=H, Z=CH₂COOH) for which conformational data are available[14] showing them to exist predominantly in the extended (*trans*-) conformation 2 in both succinic and α-methylsuccinic acid and their esters, i.e. in that conformation which possesses the minimum dipole in solution. In the free acids, strong intra- or intermolecular H-bonding exists and would cause conformational changes in both polar and nonpolar solvents, which would in turn affect the chiroptical properties of the molecule.[15] To avoid such complications, we investigated the CD of S-(−)-dimethyl α-methyl succinate (2, R=R'=Me).


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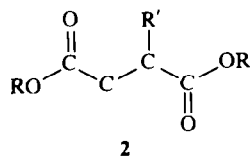
Results and discussion. CD measurements were carried out in two different solvents, 95% EtOH and cyclohexane, and at variable temperatures ranging from −20° to 38°. The data presented in Table 1 and Figs. 3(a) and (b) summarize the position, magnitude and sign of the ellipticity bands of S-(−)-dimethyl α-methyl succinate under various experimental conditions. Two Cotton effects of opposite sign were always observed in this study. The shorter wavelength band centered at 208 nm is much higher in intensity than the longer wavelength band of which the position of maximum ellipticity is shifted further to the visible range when the ratio of these two bands increases (Fig. 3). At a specified temperature, e.g. 20°, the shorter wavelength band increases in intensity in a polar solvent such as ethanol, whereas the longer wavelength band decreases. For measurements at different temperatures, it can be seen that, in both solvents, the large band increases at the expense of the small when temperature is lowered, and vice versa. Such solvent and temperature effects observed implied that the two bands are closely interrelated and are probably associated with a single electronic transition. The best possible explanation for these findings would be the existence of an equilibrium between two or more conformers of this ester in solution. According to the "bent bond" or "banana type" concept[16] of the double bond, a three fold barrier to rotation around the Cα–COOR bond is generally assumed and a staggered conformation as shown in 1 is ordinarily favored on energy consideration. For the three most likely conformers, 1a, 1b and 1c, 1c is considered the least stable on steric grounds and 1a is regarded as the preferred conformer. If these three rotamers are projected into the back octant of Fig. 1, 1a contributes a negative sign, 1b a positive sign, and 1c a negligible contribution to the n → π* transition of the ester. Combining the results from the steric point of view and the application of the octant rule, it may be concluded that 1a is the conformation responsible for the 207 nm band and 1b is that associated with the long wavelength band.

		X =	Y =	Z =
	1a	H	CH₃	CH₂COOCH₃
	1b	CH₂COOCH₃	H	CH₃
	1c	CH₃	CH₂COOCH₃	H
	1d	CH₂COOR	H	R'
	1e	H	R'	CH₂COOR
	1f	R'	CH₂COOR	H

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Table 1. Circular dichroism of S-(−)-dimethyl α-methylsuccinate (2, R=R′=CH₃)

solvent	temperature (°C)	$[\theta]_{208}$	$[\theta]_{240}$ (nm)
Cyclohexane	10	−2240	+38 (242)
'	20	−2070	+44 (240)
'	30	−1880	+53 (238.5)
''	38	−1680	+61 (237.5)
95% EtOH	−20	−3010	+5.9 (244)
''	−10	−2790	+7.0 (244)
''	−0	−2550	+9.2 (243)
''	20	−2200	+12.8 (242)
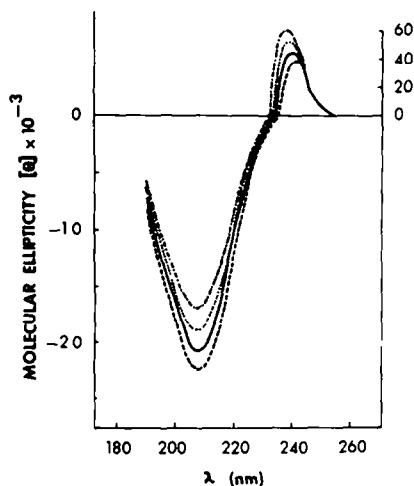
Fig. 3(a) Circular dichroism of S-(−)-dimethyl α-methyl-succinate in cyclohexane at 10°C (----), 20°C (——), 30°C (·····) and 38°C (-·-·-).
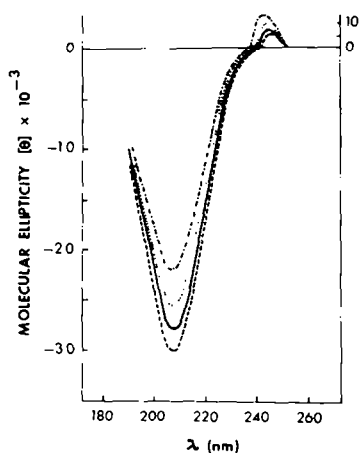
Fig. 3(b) Circular dichroism of S-(−)-dimethyl α-methyl-succinate in 95% ethanol at −20°C (----), −10°C (——), 0°C (·····) and 20°C (-·-·-).

Extrapolation of the data in Table 1 to a zero value of the ellipticity for the 235 nm band (Fig. 4) in both 95% ethanol and cyclohexane gives an approximate magnitude for the CD of the lower wavelength band corresponding to
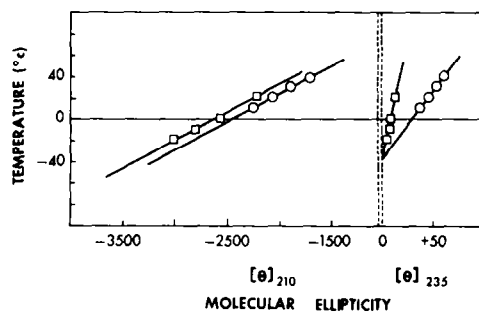
Fig. 4. Temperature-dependence of S-(−)-dimethyl-α-methyl succinate in cyclohexane (-O-O-) and in 95% ethanol (-□-□-).

100% population of that conformer responsible for this band. For both solvents, the extrapolated value is −3300 ± 100. Calculation of the approximate free energy difference between the two conformers at 20° gives ΔG = − 400 cal/mole in 95% ethanol for the equilibrium (235 conformer⇌210 nm conformer). In cyclohexane, the corresponding value of ΔG is −310 cal/mole.

At about the same time as this work was in progress, the CD of four α-alkyl succinic acids (2, R=H, R′ = ethyl, butyl, isopropyl, and cyclohexyl) in water was reported.[13] A single ellipticity band near 210 nm was shown and no longer wavelength band was discerned.[13] Since these findings were not in agreement with our results on dimethyl α-methyl succinate, we re-examined a series of nine of these acids (2, R=H, R′ = methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, cyclohexyl and isobutyl). The results of the CD measurements in 95% EtOH are summarized in Table 2. All the acids except S-(−)-isopropyl and S-(−)-cyclohexyl succinic acid showed both 210 nm and 235 nm bands of opposite sign, exactly as in the methyl ester (above). The magnitude of the higher wavelength band decreased with increasing size of the α-substituent R′ and, at the same time, the rotational contribution of the R′ group to the shorter wavelength band increases from methyl to isopropyl. The absence of the long wavelength band for S-(−)-isopropyl and S-(−)-cyclohexyl succinic acids can best be explained on the basis that these two acids both possess α-branched substituents which would result in higher energy barriers for rotation around the Cₐ–COOH bond and thus they exist preferentially in the lowest-energy conformation. As there is no mutual reduction of rotational strength due to another oppositely signed long wavelength band,[17] the

Table 2. Circular dichroism of S-(−)-α-alkylsuccinic acids (2, R=H, R′ = Alkyl) in 95% EtOH

R′	$[\theta]_{210}$(nm)	$[\theta]_{235}$(nm)
Methyl	−1840 (208)	+40 (239)
Ethyl	−2300 (209.5)	+13 (244.5)
Propyl	−2380 (209)	+15.5 (243.5)
n-Butyl	−2290 (209)	+11.7 (244)
n-Pentyl	−2490 (209.5)	+14.5 (246)
n-Hexyl	−2430 (210)	+13.7 (245)
Isopropyl	−4240 (211.5)	0
Cyclohexyl	−3660 (210.5)	0
Isobutyl	−2120 (208.5)	+42.7 (241)

apparent maximum ellipticity of these two acids is much higher than that of all other acids in the series (Table 2). The results obtained here offer a further support to the argument given earlier for the ester, i.e. a conformational equilibrium exists in solution and from the analogous conformational analysis of S-(−)-dimethyl α-methyl succinate, the most favored conformation responsible for the 210 nm band is (1, X=H, Y=R′, Z=CH₂COOH) and that responsible for the 235 nm band is (1, X=CH₂COOH, Y=H, Z=R′).

α-Halo succinic acids and esters

To avoid possible inter- or intramolecular H-bonding which would in turn affect the chiroptical properties of the acids in solution, we investigated the CD of S-(−)-

Table 3. Circular dichroism of S-(−)-dimethyl α-chlorosuccinate (2, R=CH₃, R′ = Cl) at 20°

Solvent	$[\theta]_{222}$	$[\theta]_{lowest\ wavelength\ measured\ (nm)}$
cyclohexane	−8460	+3550 (185)
95% EtOH	−4370	+1810 (186)
H₂O containing 10% EtOH	−3080	+1590 (185)

dimethyl α-chloro and α-bromo succinates in both 95% EtOH[18] and in cyclohexane. The position and magnitude of the CD absorptions are summarized in Tables 3 and 4. In all three solvent systems used, it was not found possible to reach the lower wavelength CD maximum of S-(−)-dimethyl α-chloro succinate even at 185 nm. Although two oppositely signed Cotton effects are demonstrated for this compound, the lack of quantitative data on the position and magnitude of the low-wavelength ellipticity, makes it impossible to draw any significant conclusion from such measurements. However, in the case of S-(−)-dimethyl α-bromo succinate, two CD maxima with opposite sign can be definitely located. The lower wavelength band, in contrast to the findings for α-methyl succinate, is much smaller in intensity than the oppositely signed long wavelength band. Variable temperature CD measurements also show a different trend of behavior: both bands increase in intensity with decreasing temperature. This strongly suggests that, unlike its α-methyl substituted analogue, S-(−)-dimethyl α-bromo succinate exhibits two different optically active transitions in the spectrum range measured. One possible explanation is that the lower wavelength CD is due to the n → σ* transition[19] of C-Br and the higher wavelength CD is due to the n → π* transition of the carboxyl group. If the same argument is applied to the α-chloro ester, it would also explain our inability to see the low wavelength CD maximum, since the n → σ* transition of C-Cl is known[20] to be at much lower wavelength. It has been shown by UV measurements[21] that axial α-bromo ketones may undergo a red shift of ~28 nm while axial α-chloroketones[22] show a red shift of ~14-25 nm in relation to the parent ketone. As an extension of this α-haloketone rule, we propose that the higher wavelength band of α-bromo and α-chloro esters is an n → π* transition shifted 15-25 nm to the red by the "axial" position of the halogen α-substituent. This corresponds to a preferred conformation (1, X=H, Y=Br or Cl, Z=CH₂COOMe) in which the Cα–Cβ bond eclipses the carbonyl oxygen. For this conformation, the corresponding octant projection in Fig. 2 would result in a negative CD as observed. Another possible conformation suggested from conformational analysis[23] of chloroacetaldehyde and bromoacetaldehyde is that in which the halogen eclipses the carbonyl double bond (1, X=CH₂COOMe, Y=H, Z=Cl or Br). The corresponding octant projection, however, shows it would give a positive CD, opposite to that observed. Also, solvent effects indicated that the long wavelength band increases in intensity with decreasing polarity of the

Table 4. Circular dichroism of S-(−)-dimethyl α-bromosuccinate (2, R=CH₃, R′ = Br)

Solvent	Temperature (°C)	$[\theta]_{235}$	$[\theta]_{202.5}$
cyclohexane	+10	−10600	+1065
	+20	−10250	+ 820
	+30	−9820	+ 740
	+38	−9530	+ 570
95% EtOH	−40	−10220	+ 730
	−20	−9490	+ 420
	0	−8700	+ 230
	+20	−8160	+ 90

solvent, which implies that the conformation responsible for this CD band is less polar in nature and therefore corresponds to (1, X=H, Y=Br or Cl, Z=CH$_2$COOMe) and not to the other conformer.

Saturated alkyl bromides are known[24] to give an optically active absorption near 200 nm. On the basis of UV measurements, this absorption is assigned as an n$\rightarrow\sigma^*$ transition of C-Br. The magnitude and position of the CD band are in exact agreement with those of the low wavelength CD observed for the α-bromo succinate. To investigate the effect of temperature on this n$\rightarrow\sigma^*$ transition, we carried out CD measurements of R-(−)-2-bromooctane at various temperatures (Table 5). Surprisingly, examination of the CD results revealed that the ellipticity band actually increases in intensity with decreasing temperature in both solvents used. Such observations further confirm our earlier proposed assignment of the 203 nm band of α-bromo succinate as primarily derived from the n$\rightarrow\sigma^*$ transition of C-Br.

While this work was in progress, the CD of L-(−)-α-chloro-succinic acid in water was reported[13] to give a positive CD maximum at 200 nm and a negative CD maximum at 222 nm. Since this did not agree with our results on S-(−)-dimethyl α-chloro succinate, we examined both L-(−)-α-chloro and L-(−)-α-bromo succinic acids in 95% EtOH and in water (Table 6). The results fully confirmed our previous conclusions reached for the corresponding dimethyl esters. Firstly, the CD in 95% EtOH was consistently larger than that in water for the same reason as in the esters. Secondly, for the chloro acid, it was not possible to record the low wavelength CD maximum in either alcohol or water. Our conclusions are therefore that the α-halo acids and esters exist in the same conformation (1, X=H, Y=Br or Cl, Z=CH$_2$COOR) in which the C$_\alpha$–C$_\beta$ bond is eclipsed by the C=O bond. This is confirmed by the agreement with the "axial haloketone rule" shift in wavelength of the n$\rightarrow\pi^*$ absorption maximum, by the fact that the octant rule is obeyed for this

conformation to give the correct CD sign but not for the alternative one (1, X=CH$_2$COOR, Y=H, Z=Cl or Br),[25] and by the effects of solvent polarity changes.

α-Hydroxy acids and esters

It was shown[5] that the ORD spectra of α-hydroxy acids of the S configuration gave a single positive Cotton effect at ca. 215 nm due to the n$\rightarrow\pi^*$ transition of the carboxyl group. Anand and Hargreaves reported[6] for S-(+)-lactic acid a weak negative CD band in the 245 nm region as well as the expected strong positive CD maximum at lower wavelength. Since the CD spectrum in alkaline solution showed no negative Cotton effect, they ascribed the band at 245 nm to the n$\rightarrow\pi^*$ transition, and the strong positive maximum at 210 nm to other including $\pi\rightarrow\pi^*$, transitions of the molecule. However, Barth et al. attributed both CD bands to the n$\rightarrow\pi^*$ transition and interpreted their data by assuming that each band is associated either with different rotamers or with different solvated species. The weak 240 nm band was also found to be present in other α-hydroxy acids, their esters, and their O-methyl ethers[9,13] and was thus not due to intra- or intermolecular H-bonding. At alkaline pH values, the 240 nm CD disappeared while an unpredictable change occurs in the magnitude of the CD band at 215 nm. Listowsky et al.[13] showed that, in general, an increase in the ratio of the magnitude of the long wavelength ellipticity compared with that of the short wavelength ellipticity is observed for the α-hydroxy acids in the nonaqueous solvents; i.e. in nonpolar solvents the contribution due to the 240 nm band increases. They also observed that an increase in temperature induces an increase in the intensity of the long wavelength band near 240 nm and a concomitant decrease in the band near 210 nm, and a decrease in temperature induces the opposite effect. This behavior implies that the two bands are closely interrelated and are probably associated with a single electronic transition. On the basis of the solvent and temperature studies, they assumed that the most stable conformation is that in which the hydroxy substituent is eclipsed by the C=O bond (1, X=CH$_2$R, Y=H, Z=OH) and that this rotamer is responsible for the 210 nm band. It was further suggested that the conformer of structure (1, X=H, Y=OH, Z=CH$_2$R) generates the longer wavelength band.

Results and discussion. The CD of S-(−)-dimethyl α-methoxy succinate was examined over a temperature range between +38 and −40° in 95% EtOH and cyclohexane (Table 7). In both solvents, an increase in temperature resulted in an increase in the magnitude of

Table 5. Circular dichroism of R-(−)-2-bromooctane

Solvent	Temperature (°C)	$[\theta]_{203}$
Cyclohexane	+10	+860
	+20	+830
	+30	+800
	+38	+770
95% EtOH	−20	+1040
	0	+960
	+20	+900

Table 6. Circular dichroism of L-(−)-chlorosuccinic acid and L-(−)-bromosuccinic acid

2, R=H, R'=	Solvent	$[\theta]_{230}$(nm)	$[\theta]_{200}$(nm)
Cl	95% EtOH	−3970 (225)	+1530! (192)
"	H$_2$O	−2320 (223)	+1940! (191.5)
Br	95% EtOH	−8060 (235)	+160 (203.5)
"	H$_2$O	−5940 (232)	+840 (203.5)

Table 7. Circular dichroism of S-(-)-dimethyl α-methoxysuccinate

Solvent	Temperature (°C)	$[\theta]_{212}$(nm)	$[\theta]_{235}$(nm)
Cyclohexane	+10	+530	-590
	+20	+500	-620
	+36	+400	-640
95% EtOH	-40	+2760 (215)	-120 (240)
	-20	+2410 (215)	-160 (240)
	0	+2120 (215)	-200 (240)
	+20	+1850 (215)	-210 (240)

the high wavelength CD and a decrease in that of the low wavelength CD, as expected from a mixture of two conformers existing in equilibrium with each other (Fig. 5). Extrapolation of the data in Table 7 to a zero value of the ellipticity for the 235 nm band gave an approximate magnitude[26] for the CD of the lower wavelength band corresponding to 100% population of that conformation. In 95% EtOH solution, this extrapolated value of the 210 nm CD was ca. +4000. From this, it was possible to calculate an approximate free energy difference between the two conformers at 20°, $\Delta G = +100$ cal/mole for the equilibrium (240 nm conformer $\rightleftarrows$ 210 nm conformer). The smallness of the $\Delta G°$ in this case may be due to the fact that no intramolecular stabilization by H-bonding is
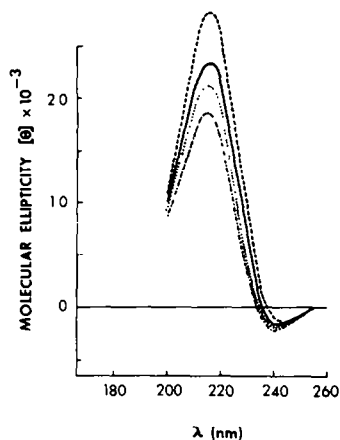

Fig. 5. Circular dichroism of S-(-)-dimethyl α-methoxy-succinate in 95% ethanol at -40°C (----), -20°C (——), 0°C (·····) and 20°C (-·-·-).

possible in the α-OMe compound examined, and also that the increased size of the methoxy group versus the hydroxy substituent will increase the population of the non-eclipsed conformer. This seems to be supported by the reported value of a $\Delta G°$ of ca. 1.1 kcal/mole in water at 25° for the two corresponding conformers of L-malic acid.[13] At lower temperatures, the percentage of the 210 nm conformer increases, suggesting that the low wavelength CD is due to (1, X=CH₂COOMe, Y=H, Z=OMe). In the octant projection (Fig. 2), the sign expected from this conformer is positive, as found experimentally.

In cyclohexane solution, the similar magnitude of the two CD maxima makes it impossible to use the same extrapolation method and obtain significant results. This

is due to the distortion in both magnitude and wavelength of the maxima caused by the overlap of two oppositely signed Gaussians when these are approximately equal.[17]

The increase in the intensity of the 210 nm CD band, and the decrease in that at 235 nm, as solvent polarity increases is in agreement with the view that rotamer (1, X=CH₂COOCH₃, Y=H, Z=OCH₃) is the most favored in polar solvents, being the one which interacts most strongly with polar solvents and is thus energetically favored through solute-solvent interactions. In low polarity solvents, the population of the other conformers should increase.

α-Amino acids and esters

In addition to the strong positive CD maximum at 200-210 nm, α-amino acid esters of the L-configuration (S) show a second (smaller) negative CD band at ca. 235 nm which (unlike the lower wavelength band) does not correspond to an observed UV transition.[3,9,10,27] The fact that α-amino acid esters containing tertiary amino groups still show the abnormal (235 nm) CD band argues against intra- or intermolecular H-bonding being responsible for this band.

Results and discussion. Our measurements on L-(+)-diethyl aspartate showed the presence of the 235 nm negative CD maximum in both 95% EtOH and cyclohexane (Table 8). The positive CD maximum in the 200-210 nm region was apparently due to a combination of two bands of the same sign, one (at lower wavelength) due to the $n \rightarrow \sigma^*$ transition of nitrogen[28] and the other due to the normal $n \rightarrow \pi^*$ transition of the carboxyl group. This was shown, e.g. by the disappearance of the lower wavelength portion ($n \rightarrow \sigma^*$) of the 200-210 nm CD band on acidification, leaving intact the normal positive band at 210 nm ($n \rightarrow \pi^*$) in the hydrochloride salt; at the same time, the 236 nm band had disappeared. For these reasons, it was not feasible to carry out temperature dependence studies on the two CD maxima corresponding to the $n \rightarrow \pi^*$ transition.

Hydrogen bonding is an important feature of the crystal structures of all the amino acids. The charged ammonium group of the zwitterion or the hydrochloride salt is an excellent H-bond donor and the carboxylate ion or the oxygen of the C=O dipole in the free acids or the esters is a good acceptor. As a result, strong H-bonds are invariably formed between these two groups, and have been found by X-ray diffraction studies.[29] Studies on amino acid conformation in the solid state, using the hydrochloride salts,[30] have shown that the amino group generally takes up the position *cis* to the C=O bond. In

Table 8. Circular dichroism of L-(+)-diethyl aspartate

Solvent	Temperature (°C)	$[\theta]_{200}$ (nm)	$[\theta]_{230}$ (nm)
Cyclohexane	+20	+5440 (202.5)	-2180 (233)
95% EtOH	-40	+2530! (192.5)	-1600 (228.5)
''	-20	+2570! (194)	-1470 (229.5)
''	0	+2650! (196)	-1320 (230)
''	+20	+2650! (197.5)	-1280 (230.5)
95% EtOH + HCl	+20	+2230 (210)	0

dilute solution in protic solvents, solvation will take the place of much of the intermolecular H-bonding. However, p-π overlap due to interaction between the amino nitrogen and the C=O bond will still tend to stabilize the amino group in the *cis* position to the C=O bond relative to the other conformers. Literature data[31] thus support the existence of α-amino acids predominantly in that conformation in which the α-amino group is close to being eclipsed by the C=O bond (1, X=CH$_2$R″, Y=H, Z=NH$_2$) for the L-configuration. As in the corresponding α-hydroxy compounds, there is also present some of the conformation (1, X=H, Y=NH$_2$, Z=CH$_2$R″), while the third possible conformer is the least favored on ground of steric repulsion. In the α-amino acid hydrochlorides, the conformer (1, X=CH$_2$R″, Y=H, Z=NH$_2$) will be even more favored due to intramolecular H-bonding, and this may explain the disappearance of the high wavelength (235 nm) negative CD band on acidification, and in the free (zwitterionic) amino acids themselves.[9,10]

In all reported observations, the CD of L-amino acids shows a positive maximum at *ca.* 215 nm, suggesting that it is due to the conformation (1, X=CH$_2$R″, Y=H, Z=NH$_2$), with a corresponding octant projection (Fig. 2) in agreement with experimental results. The conformational behavior of the α-amino acids or esters is thus very similar to that of the corresponding α-hydroxy acids of the same configuration, and it is possible that the longer wavelength band for the α-amino acids is generated by the conformer of structure (1, X=H, Y=NH$_2$, Z=CH$_2$R″).

CONCLUSION

Of the three conformers 1d, 1e and 1f, all available evidence indicates that when R′ = alkyl or halogen in 2, the preferred conformation is 1e, with the –CH$_2$COOR group eclipsed by the C=O bond, while when R′ = hydroxy, methoxy or amino in 2, they exist mainly in the conformation 1d in which the heteratom is eclipsed with the CO group. In both cases, conformation 1f appears to be the least favored, mainly on steric grounds.

In the resultant octant projection (Fig. 2) it is therefore clear that the sign of the Cotton effect for 1 will be determined solely by the position of the group X and Y in the back octants. Since in conformations, 1d and 1e, one of the two groups, X or Y is always H, accordingly the sign is actually determined simply by the position of the other group. This octant projection thus predicts the expected sign of the ellipticity of the n→π* transition in the 200–250 nm region for any α-alkyl, halo, hydroxy, alkoxy, or amino substituted succinic acids or esters 2. These conclusions also appear to apply to the simple alkanoic acids or esters (1, X=CH$_2$R″, Y=H, Z=R′) with the same α-substituent R′, and are not in disagreement with the simple empirical rule proposed by Listowsky *et al.*[13]

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