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CIRCULAR DICHROISM OF α-DEUTERIOCARBOXYLIC ACIDS.
DISSIGNATE BEHAVIOR OF DEUTERIUM.[1]

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Summary: Positive n → π* Cotton effects were shown by (S)-2-deuteriopropionic acid, (S)-2-deuteriosuccinic acid, (R)-2-deuterioglycine and (R)-2-deuterioglycolic acid. Using an octant projection and conformational and chiroptical data, it can be shown that the deuterium substituent makes a dissignate contribution to the Cotton effect.

Recent reports on the circular dichroism (CD) of cycloalkanones owing their chirality to deuterium substitution alone have revealed that the rotational contribution of deuterium in most cases is dissignate (anti-octant).[3] The reason for this behaviour was sought[3b,f] in the low refractivity of deuterium compared to that of hydrogen and in the fact that the C-D bond length is shorter than that of the C-H bond. In a very recent theoretical study, Lightner et al.[4] showed that the rotational contribution from a C-D bond is smaller than that of the corresponding C-H bond, and concluded that the net contribution to the sign of the rotatory strength is determined by the comparatively more consignate (octant) contribution of the C-H bond that is located in an oppositely signed octant relative to the C-D bond.

We have investigated the n → π* Cotton effects (CE's) of the α-deuteriocarboxylic acids (S)-2-deuteriopropionic acid [(S)-1], (S)-2-deuteriosuccinic acid [(S)-2], (R)-2-deuterioglycine [(R)-3], and (R)-2-deuterioglycolic acid [(R)-4] in order to relate the results to a sector rule for the carboxyl chromophore, and wish to report that a deuterium substituent in the α-position of a carboxylic acid also makes a sign-reversed contribution to the CE.

Acyclic carbonyl compounds have been found[5] to have a threefold barrier to rotation around the Cα-CO bond, one of the three groups attached to Cα being syn-periplanar with the carbonyl group. In the case of straight-chain carboxylic acids the conformational possibilities are reduced due to the preference of the carbonyl group to be syn-periplanar with an alkyl group rather than with a hydrogen atom. Thus propionic acid has been shown by X-ray diffraction[6,7] and microwave spectroscopy[8] to have a virtually planar carbon-oxygen skeleton in which the methyl group is syn-periplanar with the carbonyl group. Force-field calculations on propionic acid[9] as well as NMR studies on propionaldehyde[10] support the predominance of this conformation. Succinic acid exists in the solid state in an analogous conformation, the C_α-C_β bond being syn-periplanar with the carbonyl group.[6,11] The results from several CD studies on substituted succinic acids[12] indicate that this conformation prevails also for succinic acid in solution. Glycine, either as the zwitterion or as the hydrochloride, has a preferred conformation with the protonated amino group syn-periplanar with the carbonyl group.[13,14] Intramolecular hydrogen-bonding[13] and/or electrostatic attractions[14] are believed to be responsible

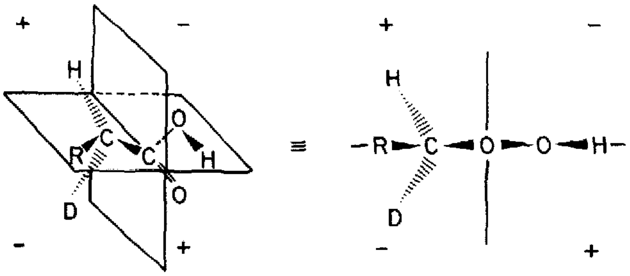

Figure 1.
Sign assignment for back octants

(S)-1 R = CH_3
(S)-2 R = CH_2COOH
(R)-3 R = NH_2
(R)-4 R = OH

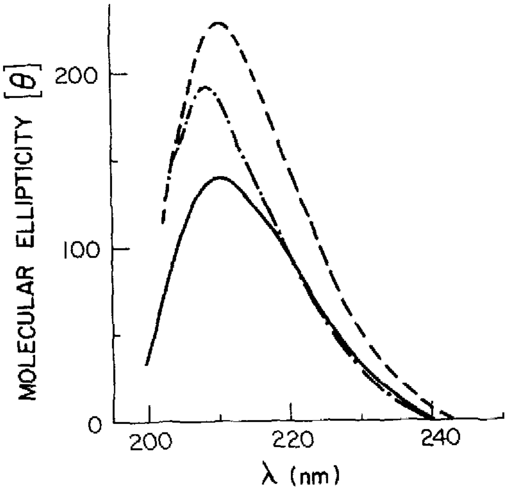

Figure 2.
Circular dichroism of
(S)-1 (——)
(S)-2 (- -) and
(R)-3 (- · -·).

for the predominance of this conformation. Similarly, glycolic acid,[15] like lactic acid,[16] has a preferred conformation with the hydroxyl group *syn*-periplanar with the carbonyl group.

The absolute configuration of **1** has been determined in several independent ways,[17] and (*S*)-**1** was found to exhibit a plain positive optical rotatory dispersion (ORD) curve in water solution.[18] Cornforth *et al.*[19] established the absolute configuration of **2** by transformation of (2*S*, 3*R*)-3-deuteriomalic acid to (*R*)-**2** which in methanol solution displayed a plain negative dispersion curve. Later Englard *et al.*[20] found a positive CE for (*S*)-**2** when the ORD measurements were extended to the 200 nm region, while Listowsky *et al.* reported[12a,21] a positive CD ($[\theta]_{208}$ + 150) for (*R*)-**2** in water at pH 2.5. For (*R*)-**3**, the absolute configuration was established by deamination to (*R*)-**4**,[22] the configuration of which was confirmed both by neutron diffraction[23] and by chemical correlation with chiral 1-deuterioethanol,[24] and both (*R*)-**3** and (*R*)-**4** gave plain positive ORD curves in water.[17] A minimum molecular ellipticity of $[\theta] = +160$ can be calculated for (*R*)-**4** from the ORD data.

Craig *et al.*[12c] analyzed the chiroptical properties of α-substituted succinic acids using an octant projection. This projection also applies to α-substituted monocarboxylic acids.[25] Projection of (*S*)-**1**, (*S*)-**2**, (*R*)-**3** and (*R*)-**4** in the conformations deduced above for the undeuterated analogues as depicted in Fig. 1 clearly shows that deuterium is located in a *negative* octant whereas the observed CE's are *positive* (Fig. 2).[26] It thus appears that the sign of the observed CE's is determined by the larger rotatory contribution from the C-H bond compared to that of the C-D bond.[4] The negative CE ($[\theta]_{209}$ - 116 in isooctane) observed for (*R*)-2-deuteriopalmitic acid[27] is in excellent agreement with these results. These conclusions are further supported by the fact that (*S*)-2-methylsuccinic acid, (*R*)-alanine, and (*R*)-lactic acid, which have preferred conformations analogous[12d,14,16] to those deduced for (*S*)-**2**, (*R*)-**3**, and (*R*)-**4** respectively [the methyl group replacing the deuterium atom in (*S*)-**2**, (*R*)-**3**, and (*R*)-**4**) (Fig. 1)] all exhibit negative CE's.[12b,c,d;28]

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