Absolute Configurations of Amino-acids and other α-Substituted Carboxylates

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RECENTLY an empirical rule was proposed whereby the absolute configuration of an asymmetric α-substituted carboxylate, X, could be determined from a study of the Cotton effects shown by the *d–d* transitions of cobalt(III) complexes of the type $[Co(NH_3)_5X]^{n+1}$. Dunlop and Gillard postulated that the sign of the dominant Cotton effect for the transitions under the first ligand-field absorption band ($^1A_{1g} \rightarrow {}^1T_{1g}$) indicates the absolute configuration of the co-ordinated carboxylate: if the dominant Cotton effect "is negative, then the acid has the L-configuration related to that of L(+)-lactic acid".[1]

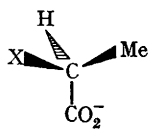
The central metal ion chromophore for complexes of the above type has a C_{4v} symmetry, and under this symmetry the lowest spin-allowed excited state is no longer triply degenerate, but is split into two levels, ^1E and $^1A_2$. According to various theoretical models the transition to the ^1E level lies at lower energy than that to the $^1A_2$.[2] From a detailed study of complexes of this type it has been found that the empirical rule as put forward is ill-conceived. The same transition does not always dominate the circular dichroism spectrum under the first ligand-field band (see Table) and, as the ^1E and $^1A_2$ symmetry transitions have different signs of Cotton effects, carboxylate ligands with the same absolute configuration can give rise to resultant Cotton effects of opposite sign in this region. Further, it seems unjustified to postulate such a general rule for α-carboxylates without considerable experimental data covering a large number of α-substituents. There is no evidence to suggest that all carboxylates with the absolute configuration (I) possessed by L(+)-lactate with X = OH, will impose the same sign of

TABLE

Absorption and circular dichroism data for the first ligand-field band of $[Co(NH_3)_5X]^{n+}$ *complexes*

Complex cation	Anion	λ_{max} abs	ϵ_{max}	λ_{max} c.d.	$\Delta\epsilon$	Assignment
(a) $[Co(NH_3)_5$L-α-alanine$]^{3+}$	ClO_4^-	500	68·4	542	+0·003	$^1A_1 \rightarrow {}^1E$
				483	−0·015	$^1A_1 \rightarrow {}^1A_2$
(b) $[Co(NH_3)_5$L-α-alaninate$]^{2+}$	ClO_4^-	501·5	74·2	540	+0·012	$^1A_1 \rightarrow {}^1E$
				480	−0·010	$^1A_1 \rightarrow {}^1A_2$
(a) $[Co(NH_3)_5$L-α-alanine$]^{3+}$	SO_4^{2-}	500	68·0	525	+0·027	$^1A_1 \rightarrow {}^1E$
(a) $[Co(NH_3)_5$L-β-phenylalanine$]^{3+}$	ClO_4^-	501	67·5	507·5	−0·091	$^1A_1 \rightarrow {}^1A_2$
(b) $[Co(NH_3)_5$L-β-phenylalaninate$]^{2+}$	ClO_4^-	501	72·2	497	−0·043	$^1A_1 \rightarrow {}^1A_1$
(a) $[Co(NH_3)_5$L-β-phenylalanine$]^{3+}$	SO_4^{2-}	500·5	67·5	507·5	+0·054	$^1A_1 \rightarrow {}^1E$
(b) $[Co(NH_3)_5$L-β-phenylalaninate$]^{2+}$ ..	SO_4^{2-}	501	71·8	495	−0·028	$^1A_1 \rightarrow {}^1A_2$
(a) $[Co(NH_3)_5$L-tryptophan$]^{3+}$	ClO_4^-	501	69·8	507·5	+0·196	$^1A_1 \rightarrow {}^1E$
(b) $[Co(NH_3)_5$L-tryptophanate$]^{2+}$	ClO_4^-	501	72·8	510	+0·208	$^1A_1 \rightarrow {}^1E$
(a) $[Co(NH_3)_5$L-tryptophan$]^{3+}$	SO_4^{2-}	501	68·9	507·5	+0·356	$^1A_1 \rightarrow {}^1E$
(a) $[Co(NH_3)_5$L-methionine$]^{3+}$	ClO_4^-	500	68·0	507·5	−0·137	$^1A_1 \rightarrow {}^1A_2$
(b) $[Co(NH_3)_5$L-methioninate$]^{2+}$	ClO_4^-	502·5	75·1	495	−0·035	$^1A_1 \rightarrow {}^1A_2$
(a) $[Co(NH_3)_5$L-leucine$]^{3+}$	ClO_4^-	501·5	68·0	505	−0·061	$^1A_1 \rightarrow {}^1A_2$
(a) $[Co(NH_3)_5$L-proline$]^{3+}$	ClO_4^-	500	68·0	525	+0·040	$^1A_1 \rightarrow {}^1E$
(a) $[Co(NH_3)_5$L-tyrosine$]^{3+}$	ClO_4^-	500·5	68·4	502	−0·071	$^1A_1 \rightarrow {}^1A_2$
(a) $[Co(NH_3)_5$D-phenylglycine$]^{3+}$	ClO_4^-	501·5	68·0	495	+0·082	$^1A_1 \rightarrow {}^1A_2$

[a] In aqueous solution; [b] In 0·92N-NH_4OH



(I)

Cotton effect on to a particular chromophore independently of the nature of X (*e.g.*, X = NH_3^+, F, Cl, Br, Et, Ph).

From this work it has been possible to correlate the absolute configuration of a series of α-amino-carboxylates with the Cotton effect of the individual transitions. Compounds with the L-configuration impose a positive sign to the $^1A_1 \rightarrow {}^1E$ and negative sign to the $^1A_1 \rightarrow {}^1A_2$ transition. This series of compounds has the NH_3^+, CO_2^-, and H groups in the same orientation relative to one another and has the variable group bound to the asymmetric centre through a carbon atom. When the amino-group is protonated, the relative rotational strengths of the ^1E and $^1A_2$ transitions are strongly dependent on the counter-ion of the complex. For the majority of the α-amino-carboxylates studied the $^1A_2$ transition was dominant when the counter-ion was perchlorate, but the rotational strength of the ^1E transition increased relative to that of the $^1A_2$ when the perchlorate was exchanged by sulphate. This strong dependence was removed when the amino-group was deprotonated.

The study of the Cotton effect of the n–π^* carboxyl chromophore has been successful in relating the absolute configurations of most of the naturally occurring α-amino-acids.[3] However, for L-tryptophan the region of the n–π^* transition is complicated by the presence of Cotton effects due to the aromatic chromophore.[4] This prohibits an unambiguous assignment of configuration. Biological methods have indicated that this isomer has the normal L-configuration but no physical technique for assigning absolute configuration has been successfully applied to this compound.[5] From a direct comparison of the c.d. spectra of the amino-acid complexes, $[Co(NH_3)_5X](ClO_4)_3$, (see Table) it would seem reasonable to conclude that naturally occurring tryptophan does not possess the normal L-configuration. However, when the perchlorate is exchanged by sulphate, the observed c.d. band increases in size which suggests that it is due to the ^1E transition and not the $^1A_2$ as indicated by its energy. An *X*-ray study of tryptophan hydrochloride utilizing anomalous dispersion[6] at present in progress in this laboratory should provide an unambiguous assignment of the compound's configuration.[7]

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