Optical Rotatory Dispersion and Circular Dichroism. Part LXXXVI.[1] Acetates and Acetamides

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C.d. curves have been recorded for about seventy secondary acetates and acetamides. Data for compounds in which the acetoxy- or acetamido-group is a substituent on a cyclohexane ring have been analysed on the assumptions (*a*) that the substituent has a strongly preferred conformation in solution and (*b*) that the contributions $\delta(\Delta\varepsilon)$ of individual C–C bonds in the vicinity of the chromophore are additive. The results substantially confirm these assumptions and appear to suggest the position of a nodal surface of the acetoxy- or acetamido-chromophore.

DURING the past ten years there have been many studies of compounds containing the carboxy- and related chromophores, and several attempts have been made to formulate semiempirical rules relating the sign and magnitude of the carboxy-group Cotton effect to the geometry of the molecule. The compounds most frequently studied have been lactones, esters in which the carboxy-group is held in a more-or-less rigid conformation, and carboxylic acids, particularly those which are significant natural products such as α-amino-acids and α-hydroxy-acids. A recent review compares the various treatments of the carboxy-chromophore which have so far been proposed.[2]

Carboxylic esters have received comparatively little attention, particularly those in which the dissymmetry of the molecule is in the alkoxy- rather than the acyl group. In an earlier paper concerning acetate esters of steroid alcohols,[3] an attempt was made to apply the sector rule, originally developed for lactones.[4] This work was hampered by instrumentation then available which did not enable the second extremum of the o.r.d. Cotton effect to be measured, but the results appeared to confirm qualitatively the predictions of the sector rule.

We now report a fresh analysis of the Cotton effects in acetates, and some corresponding substituted acetamides, based on c.d. measurements at the wavelength of maximum absorption near 212 nm.

RESULTS

C.d. data for acetates and acetamides are presented in the first two columns of Tables 1 and 2; unless otherwise indicated the measurements refer to methanolic solutions. The compounds are all esters and amides of secondary alcohols and amines, and include examples in which the substituent is in a six-membered ring, in a five-membered ring, and in a steroid side chain; derivatives of a few aliphatic secondary alcohols and amines have also been examined. The c.d. maximum for acetates occurs near 211—212 nm (range 207—217 nm); this corresponds to the maximum occurring at the same wavelength in the isotopic absorption spectrum. For amides, the c.d. maximum is near 213—214 nm (range 209—217 nm). In general, values of $\Delta\varepsilon$ are small for acetates ($<1{\cdot}5$) but larger for acetamides ($<5{\cdot}0$).

DISCUSSION

Before any attempt can be made to rationalise the observed Cotton effects of compounds containing a flexible chromophore, some evidence regarding conformation is essential. For compounds in which an acetate group is attached to a cyclohexane ring, n.m.r.[5] and i.r.[6] studies, as well as *X*-ray crystallographic analysis in the solid state,[7] indicate that the preferred conformation is that in which the C=O of the acetate group eclipses the bond from carbon to the secondary hydrogen atom concerned; the same conformation has also been found (n.m.r.) in steroid acetamides[8] (see Figure). We start from the assumption that this conformation is preferred in solution and the correlation of the data given below suggests that the assumption is justified.

In a recent survey of the c.d. of ketones,[9] an empirical analysis of the extensive data has been used to assign to each bond in an array of cyclohexane rings, the contribution made by that bond to the observed Cotton

[1] Part LXXXV, P. M. Johnson, J. Watkins, P. M. Scopes, and B. M. Tracey, *Ann. rheum. Dis.*, 1974, **33**, 366.
[2] W. Klyne and P. M. Scopes, 'The Carboxyl and Related Chromophores,' in 'Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism,' ed. F. Ciardelli and P. Salvadori, Heyden, London, 1973.
[3] J. P. Jennings, W. P. Mose, and P. M. Scopes, *J. Chem. Soc.* (*C*), 1967, 1102.
[4] J. P. Jennings, W. Klyne, and P. M. Scopes, *J. Chem. Soc.*, 1965, 7211.
[5] C. R. Narayanan and M. R. Sarma, *Tetrahedron Letters*, 1968, 1553.
[6] C. R. Narayanan, M. R. Sarma, T. K. K. Srinivasan, and M. S. Wadia, *Canad. J. Chem.*, 1969, **47**, 1601.
[7] A. McL. Mathieson, *Tetrahedron Letters*, 1965, 4137.
[8] C. R. Narayanan and B. M. Sawant, *Tetrahedron Letters*, 1971, 1321.
[9] D. N. Kirk and W. Klyne, *J.C.S. Perkin I*, 1974, 1076.

TABLE 1

C.d. of acetates (in methanol)

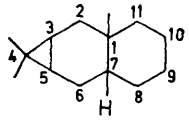
A Acetates on a *trans*-fused six-membered ring

	Δε	λ/nm	Contributing bonds	Bond values	Total
3β-Acetoxy-5α-pregnane	−0·11m	212	*bab*	−0·1	−0·1
17α-Acetoxy-18-nor-D-homo-5α-androstane	+0·07m	210	*dad*	+0·1	+0·1
(2*R*,9*R*,10*R*)-2-Acetoxydecalin	+0·03m	214	*dad*	+0·1	+0·1
(3*S*,6*R*,9*R*,10*R*)-6-Acetoxy-3-isopropyl-9-methyldecalin	0·00	210	*dad*	+0·1	+0·1
3α-Acetoxy-5α-cholestane	0·00	210	*dcd*	0·0	0·0
(3*S*,6*S*,9*R*,10*R*)-6-Acetoxy-3-isopropyl-9-methyldecalin	−0·05m	209	*dcd*	0·0	0·0
2α-Acetoxy-5α-cholestane	−0·29m	207	*bab*	−0·1	−0·25
			bac	−0·15	
17α-Acetoxy-D-homo-5α-androstane	+0·22m	210	*dad*	+0·1	+0·25
			dac	+0·15	
6α-Acetoxy-5α-cholestane	−0·56m	214	*bac*	−0·15	−0·65
			bd	−0·50	
4α-Acetoxy-5α-cholestane	+0·74m	210	*dac*	+0·15	+0·75
			dad	+0·10	
			db	+0·50	
(3*S*,5*S*,9*S*,10*S*)-5-Acetoxy-3-isopropyl-9-methyldecalin	−0·54m	215	*bac*	−0·15	−0·75
			bab	−0·10	
			bd	−0·50	
(1*S*,9*S*,10*R*)-1-Acetoxydecalin	−0·62m	210	*bab*	−0·10	−0·60
			bd	−0·50	
4α-Acetoxy-5α-oestrane	+0·85m	210	*dad*	+0·10	+0·60
			db	+0·50	
4β-Acetoxy-5α-cholestane	−0·63m	217	*bcb*	0·0	−0·70
			bd	−0·50	
			bca	−0·20	
6β-Acetoxy-5α-cholestane	+0·77m	212	*db*	+0·50	+0·70
			dca	+0·20	
(3*S*,5*R*,9*S*,10*S*)-5-Acetoxy-3-isopropyl-9-methyldecalin	+0·66m	214	*db*	+0·50	+0·70
			dcd	0·0	
			dca	+0·20	
2β-Acetoxy-5α-androstane	−0·15m	212	*dcd*	0·0	−0·20
			dca	−0·20	
17β-Acetoxy-D-homo-5α-androstane	+0·23m	211	*bcb*	0·0	+0·2
			bca	+0·20	
3β-Acetoxy-4,4-dimethyl-5α-cholestane	−0·80m	210	*bab*	−0·10	−0·80
			bd	−0·50	
			bc	−0·20	
17aβ-Acetoxy-D-homo-5α-androstane	−0·81m	210	*bab*	−0·10	−0·80
			bd	−0·50	
			bc	−0·20	
17aα-Acetoxy-D-homo-5α-androstane	+0·88m	208	*dcd*	0·0	+0·90
			db	+0·50	
			da	+0·40	
1α-Acetoxy-5α-androstane	−1·28m	213	*bcb*	0·0	−1·30
			bd	−0·50	
			ba	−0·40	
			bdc	−0·40	
7α-Acetoxy-5α-cholestane	+0·87m	210	*db*	+0·50	+0·90
			dbc	+0·40	
7β-Acetoxy-5α-cholestane	−1·24m	212	*bd*	−0·50	−1·20
			bda	−0·70	
11α-Acetoxy-D-homo-5α-androstane	+1·27m	210	*db*	+0·50	+1·45
			dbc	+0·40	
			bac	−0·15	
			dba	+0·70	
3β, 12α-Diacetoxy-5α-spirostan	−0·36m	210	*bd*	−0·50	−1·40
			ba	−0·40	
			bdc	−0·40	
			bab (3βOAc)	−0·10	
12α-Acetoxy-5β-cholane	−1·41m	209	*bd*	−0·50	−1·30
			ba	−0·40	
			bdc	−0·40	

TABLE 1 (*Continued*)

	Δε	λ(nm)	Contributing bonds	Bond values	Total
3β, 12β-Diacetoxy-5α-spirostan	+0·55m	210	*db*	+0·50	
			dc	+0·20	+1·3
			dba	+0·70	
			bab (3βOAc)	−0·10	
12β-Acetoxy-5β-cholane	+1·09m	210	*db*	+0·50	
			dc	+0·20	+1·40
			dba	+0·70	
B Acetates on a *cis*-fused six-membered ring					
3α-Acetoxy-5β-cholestane	+0·05m	210	*dad*	+0·10	+0·10
3β-Acetoxy-5β-cholestane	−0·17m	212	*bcb*	0·0	0·0
9β-Acetoxy-tricyclic derivative *	+0·05m	220	*dac*	+0·15	+0·15
9β-Acetoxy-8α-methyl-tricyclic derivative *	+0·48m	218	*dac*	+0·15	+0·65
			db	+0·50	
10α-Acetoxy-8α-methyl-tricyclic derivative *	+0·10m	216	*dac*	+0·15	+0·15
9α-Acetoxy-8α-methyl-tricyclic derivative *	−0·75m	222	*bd*	−0·50	−0·70
			bca	−0·20	
10β-Acetoxy-8α-methyl-tricyclic derivative *	+0·12m	219	*bca*	+0·20	+0·20
8β-Acetoxy-tricyclic derivative *	+0·15m	218	*dad*	+0·1	
			da	+0·40	+0·30
			dca	−0·20	
C Acetates on a five-membered ring					
15α-Acetoxy-5α-androstane	−1·88m	207			
16α-Acetoxy-5α-pregnane	+1·09m	213			
3β,16α-Diacetoxy-5α-androstane	+0·24m	210			
3β,16β-Diacetoxy-5α-androstane	+0·10m	211			
3β,17α-Diacetoxy-5α-androstane	−0·21m	215			
17β-Acetoxy-5α-androstane	−0·20m	210			
3β,17β-Diacetoxy-5α-androstane	−0·33m	207			
D Acyclic acetates					
(i) Steroid side chain					
(20*S*)-3α,20α-Diacetoxy-5α-pregnane	−1·10m	211	*bd*	−0·50	
			ba	−0·40	
			bac	−0·15	−1·15 †
			bab	−0·10	
			dcd (3αOAc)	0·0	
(20*S*)-3α,20α-Diacetoxy-5β-pregnane	−1·05m	208	as above, replace *dcd* with *dad*	+0·10	−1·05 †
(20*R*)-3α,20β-Diacetoxy-5α-pregnane	+1·53m	212	*db*	+0·50	
			dba	+0·70	
			dbc	+0·40	
			da	+0·40	+2·1 †
			dad	+0·10	
			dcd (3αOAc)	0·0	
(20*R*)-3α,20β-Diacetoxy-5β-pregnane	+1·63m	212	as above, replace *dcd* with *dad*	+0·10	+2·2 †
(ii) Simple aliphatic					
(2*R*)-2-Acetoxybutane	+0·29m	210			
(2*R*)-2-Acetoxypentane	+0·45m	209			
(2*R*)-2-Acetoxyhexane	+0·41m	210			
(2*R*)-2-Acetoxyheptane	+0·46m	209			
(2*R*)-2-Acetoxyoctane	+0·37m	210			

* Acetoxy-group substituted in the 1,4,4-trimethyltricyclo[5,4.0.0^{3,5}]undecane skeleton; steroid conventions used for stereochemistry; see F. Fringuelli, A. Tattichi, F. Fernandez, D. N. Kirk, and P. M. Scopes, *J.C.S. Perkin I*, 1974, 1103.



† Bond values are only approximate; see text.

effect. A similar analysis has now been developed for acetates, on the basis of the conformation described above.

Description of Bonds.—The Figure shows the array of bonds which are thought to be significant for an acetate group attached to a cyclohexane ring. The symmetry plane of the carboxy-group divides the space around the chromophore into two enantiomeric regions and, for simplicity, only those bonds in front of the acetate group are shown. These bonds can all be described by a modification of the tetrahedral co-ordinate system recently suggested for specifying atomic positions and bond directions in a diamond network.[10] Four mutually tetrahedral directions are defined from the origin C-1; direction '*a*' is that of the X–C(1) bond, direction '*c*' is that of the C(1)–H bond; the directions defined by bonds C(1)–C(2) and C(1)–C(6) are labelled '*b*' and '*d*.'

[10] D. Rogers and W. Klyne, *Tetrahedron Letters*, 1972, 1441.

TABLE 2

C.d. of acetamides (in methanol)

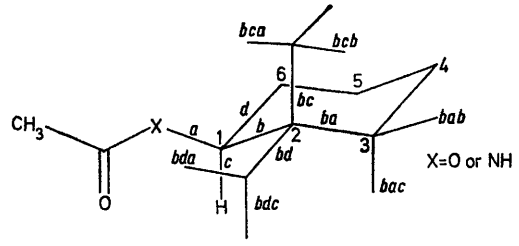
	Δε	λ/nm	Contributing bonds	Bond values	Total
A Acetamides on a *trans*-fused six-membered ring					
3β-Acetamido-5α-cholestane	−0·60	212	*bab*	−0·50	**−0·50**
3β-Acetamido-5α-androstane	−0·35	212	*bab*	−0·50	**−0·50**
3α-Acetamido-5α-cholestane	−0·00	210	*dcd*	−0·1	−0·1
3α-Acetamido-5α-androstane	−0·13	218	*dcd*	−0·1	−0·1
2α-Acetamido-5α-cholestane	−1·13m	214	*bab*	−0·50	**−1·10**
			bac	−0·60	
6α-Acetamido-5α-cholestane	−0·64m	216	*bac*	−0·60	**−0·80**
			bd	−0·20	
6α-Acetamido-5α-androstane	−0·46m	215	*bac*	−0·60	**−0·80**
			bd	−0·20	
4α-Acetamido-5α-cholestane	+1·45m	213	*dac*	+0·60	**+1·30**
			dad	+0·50	
			db	+0·20	
4α-Acetamido-5α-androstane	+1·58m	213	*dac*	+0·60	**+1·30**
			dad	+0·50	
			db	+0·20	
4β-Acetamido-5α-cholestane	+0·87m	216	*bcb*	+0·10	**+1·50**
			bd	−0·20	
			bca	+1·60	
4β-Acetamido-5α-androstane	+0·89m	215	*bcb*	+0·10	**+1·50**
			bd	−0·20	
			bca	+1·60	
6β-Acetamido-5α-cholestane	−1·84m	215	*db*	+0·20	**−1·40**
			dca	−1·60	
6β-Acetamido-5α-androstane	−2·11m	214	*db*	+0·20	**−1·40**
			dca	−1·60	
2β-Acetamido-5α-cholestane	−1·60m	213	*dcd*	−0·10	**−1·70**
			dca	−1·60	
3β-Acetamido-4,4-dimethyl-5α-cholestane	−0·89m	209	*bab*	−0·50	**−0·90**
			bd	−0·20	
			bc	−0·20	
17aβ-Acetamido-3β-acetoxy-D-homo-5α-androstane	0·0	215	*bab*	−0·50	**0·0**
			bd	−0·20	
			bc	+0·80	
			bab (3βOAc)	−0·10	
7α-Acetamido-5α-cholestane	+2·55	212	*db*	+0·20	**+2·60**
			dbc	+2·40	
1α-Acetamido-5α-cholestane	−3·85	213	*bcb*	+0·10	**−3·90**
			bd	−0·20	
			bdc	−2·40	
			ba	−1·40	
7β-Acetamido-5α-cholestane	−3·55m	214	*bd*	−0·20	**−4·10**
			bda	−3·90	
7β-Acetamido-5α-androstane	−4·42m	210	*bd*	−0·20	**−4·10**
			bda	−3·90	
11α-Acetamido-5α-androstane	+5·61m	212	*db*	+0·20	**+5·90**
			dbc	+2·40	
			dba	+3·90	
			bac	−0·60	
11β-Acetamido-5α-androstane	−5·98m	213	*bd*	−0·20	**−8·10**
			bdc	−2·40	
			bda	−3·90	
			dca	−1·60	
12β-Acetamido-3β-acetoxy-5α-spirostan	+1·48	212	*db*	+0·20	**+3·20** *
			dba	+3·90	
			dc	−0·80	
			bab (3βOAc)	−0·10	
C Acetamides on a five-membered ring					
17α-Acetamido-5α-androstane	−3·40m	215			
17β-Acetamido-5α-androstane	+1·94m	218			
D Acyclic acetamides					
20α-Acetamido-5α-pregnane	−3·72m	210	*bd*	−0·25	**−2·75** *
			ba	−1·40	
			bac	−0·60	
			bab	−0·50	

TABLE 2 (*Continued*)

	Δε	λ(nm)	Contributing bonds	Bond values	Total
20α-Acetamido-3α-hydroxy-5β-pregnane	−3·10m	208	*bd*	−0·25	
			ba	−1·40	
			bac	−0·60	−2·75 *
			bab	−0·50	
20β-Acetamido-5α-pregnane	+4·57m	208	*db*	+0·25	
			dba	+3·90	
			da	+1·40	+8·45 *
			dad	+0·50	
			dbc	+2·40	

* Bond values are only approximate; see text.

The latter two bonds are by definition enantiomeric in their relationship to the chromophore, a fact which is conveniently symbolised by the enantiomeric shape of the letters '*b*' and '*d*.'



Significant bonds for an acetoxy-group (X = O) or an acetamide-group (X = NH) attached to a cyclohexane ring. The symmetry plane includes the carboxy-chromophore and bisects the cyclohexane ring; for bonds in front of the symmetry plane the first letter of the descriptive code is *b*, for the corresponding bonds behind the plane the first letter is *d*

The geometrical relationship of any bond with the chromophore can now be uniquely described by a series of symbols representing the shortest bond-path from C(1), each bond being defined by its directional symbol until the bond in question is reached. Thus the bond C(2)–C(3) can be described as '*ba*,' and the axial bond at C(2) as '*bc*.' Bonds behind the carboxy-group symmetry plane (Figure) can be described by the same symbols with *d* replacing *b*; *e.g.* the bond C(5)–C(6) is *da*. The description of every significant type of bond βγ or γδ to C(1) is shown in the Figure.

Acetates.—The third column of Table 1A lists the significant bonds which may contribute to the observed dichroism of a particular molecule. Significant bonds are necessarily restricted to those which are *not* compensated by a symmetrically placed bond on the other side of the acetate symmetry plane; they appear to be limited to those bonds which are not more than three bonds removed from the secondary carbon atom C(1). The additivity of bond contributions [9] is assumed.

The simplest molecules are those which contain only one significant dissymmetrically placed bond. For example, 3β-acetoxy-5α-pregnane and geometrically related compounds have only one uncompensated bond within the limits defined, a *bab* bond [C(5)–C(6)]. The average Δε value for the five compounds listed is −0·1 and we therefore ascribe a bond value of −0·1 to *bab*, and a value of +0·1 to *dad* bonds. Similarly, a *bcb* bond is assigned a zero value (see Table). 2α-Acetoxy-5α-cholestane and 17α-acetoxy-D-homo-5α-androstane are quasienantiomeric. Both contain significant bonds of the *bab* and *bac* types, and by incorporating the value of *bab* already mentioned, a value of −0·15 is deduced for a *bac* bond.

In this way, by successive consideration of molecules with an increasing number of significant bonds, a set of inter-related bond values has been deduced. The order in which the values were calculated follows the order of section A of Table 1. Bond values deduced in this way give consistent results within the groups of compounds studied apart from one anomaly concerning the bond *bca*. From the Δε values for 4β-acetoxy-5α-cholestane, 6β-acetoxy-5α-cholestane, and (3*S*,5*R*,9*S*,10*S*)-5-acetoxy-3-isopropyl-9-methyldecalin, a value −0·20 is deduced for *bca* and consequently a value of +0·20 for *dca*. From the Δε values of 2β-acetoxy-5α-androstane and 17β-acetoxy-D-homo-5α-androstane, the bond values deduced are of the reverse sign, +0·20 for *bca* and −0·20 for *dca*. It may be significant that values for all other bonds which appear in front of the carboxy-group symmetry plane as drawn in the Figure are of negative sign, and therefore values for all bonds behind the symmetry plane are positive. The anomalous bond for which two different values can be deduced lies close to the alkoxy-oxygen atom. We suggest that this bond may be near a further and so far undefined nodal surface of the carboxy-chromophore, such that a small difference in conformation in the two classes of compounds causes the bond to lie more on one side or the other of the surface.

The signs of the bond values deduced are in agreement with those predicted by the sector rule for this region of space, in our earlier work on acetates.[3] (The bonds drawn in front of the chromophore symmetry plane in the Figure would be the front upper right region of negative contribution, following the sector rule.[4])

Five of the compounds listed in Table 1A were not used in the derivation of bond contributions. The 11α-acetoxy-D-homo-steroid is the only acetate we examined which has significant bonds on *both* sides of the chromophore symmetry plane: it shows good agreement between calculated and experimental Δε values. For the four 12-acetoxy-compounds, significant bonds are the C(13)–C(17) bond, the 13β-methyl group, and the near parts of the side chain, none of which correspond precisely in geometry to the bonds in a perfect fused-chair system of cyclohexane rings because the five-membered ring D is involved. Calculated Δε values for

the 12-acetates have the expected signs but the magnitudes, particularly for the spirostan derivatives, show above average deviations.

The compounds listed in Table 1B are those in which an acetoxy-group is substituted in a cyclohexane ring *cis*-fused to one or more other rings. Experimental $\Delta\varepsilon$ values (second column) are compared with calculated values obtained by summing contributions from significant non-compensated bonds, as deduced in Table 1A. For the first five compounds listed, the calculated $\Delta\varepsilon$ values are all of the correct sign and order of magnitude. The remaining three decalin derivatives all include the bonds *bca*/*dca* which, in the *trans*-series, were shown to make contributions of anomalous sign. The first of these three compounds is of the same geometric type as 4β- and 6β-acetoxy-5α-steroids, in that the hydrogen atom at C-2 of the 1,3-diaxial grouping is *trans* to the acetoxy-groups. The latter two compounds are similar to the 2β-acetoxy-5α- and 17β-acetoxy-D-homo-steroids and have a *cis*-hydrogen atom at C-2 of the 1,3-diaxial grouping. Introduction of the appropriate bond values for these three compounds gives calculated $\Delta\varepsilon$ values of the same sign and order of magnitude as the experimental values.

Table 1C gives c.d. data for a limited number of compounds in which the acetoxy-group is directly attached to a five-membered ring. Bond values deduced for acetates substituted in a cyclohexane network would not be expected to apply to the cyclopentane series, but a connection appears to exist between the sign of the Cotton effect and the sense in which the five-membered ring is skewed. The chiroptical properties of cyclopentanones have previously been related to the sense of skew of the five-membered ring; for the seven acetates studied, the relationship between the sign of the Cotton effect and the twist of the ring appears to reverse that found for ketones.[11]

Data for 20α- and 20β-acetoxypregnanes and for some simple acyclic esters are listed in Table 1D. Again no direct comparison with cyclohexane derivatives is possible but it may be significant that addition of bond values closest in character to those actually found in the 20-acetoxypregnanes, if we assume the usual preferred conformation of the pregnane side chain,[12] gives values of $\Delta\varepsilon$ of the same sign and order of magnitude as the experimentally determined value, *i.e.* negative and positive Cotton effects corresponding to (20*S*)(20α) and (20*R*)(20β), respectively.

The 2(*R*)-acetoxyalkanes, all show positive Cotton effects with an average $\Delta\varepsilon$ value of +0·40. This compares well in sign and magnitude with the bond value +0·50 deduced for the *db* bond in the diamond network and must presumably be attributed mainly to the C(3)–C(4) bond of a 2(*R*)-acetoxyalkane, with a fully extended conformation of the hydrocarbon chain, although other conformations of higher energy must presumably contribute in lesser degree.

[11] W. Klyne, *Tetrahedron*, 1961, **13**, 29; *Bull. Soc. chim. France*, 1960, 1396.

Acetamides.—The c.d. data for steroid acetamides can be used in the same way to deduce a set of bond values for the array of C–C bonds significant for an acetamide group attached to a cyclohexane ring. The experimental $\Delta\varepsilon$ values and the bond values deduced from them are presented in Table 2A; c.d. data for a few acetamides substituted in a five-membered ring and for some acyclic acetamides are also included in Table 2 (sections C and D).

The acetamide bond values follow the general pattern observed for acetates with regard to sign, but with one significant difference. The bond *bca* which can make either a positive or a negative contribution to the total $\Delta\varepsilon$ value of an acetate, always has a positive value for the corresponding acetamide; conversely, the bond *bc*, which has a small negative value for acetates, appears to make a positive contribution in 17aβ-acetamido-3β-acetoxy-D-homo-5α-androstane and a negative contribution in 3β-acetamido-4,4-dimethyl-5α-cholestane. This suggests that a second nodal surface of the chromophore, which for acetates passes near the bond *bca* or *dca*, is shifted in the case of acetamides so that the *bc* or *dc* bond is in or near the nodal surface and *bca* or *dca* always lies in a positive region.

It is also interesting that the bond values for acetamides are generally four or five times larger than those for acetates. In particular, the bonds *bca*/*dca*, *bdc*/*dbc*, and *bda*/*dba*, close to the CONH chromophore contribute ±1·5—4 units to the total $\Delta\varepsilon$ value.

Computer Analysis.—One possible disadvantage of the empirical analysis described above is the successive deduction of bond values, which necessarily lays proportionately greater emphasis on the experimental data for compounds with only one or two significant bonds and gives much less weight to data for compounds with many significant bonds. We have therefore checked our empirical values by a simple computer analysis, using a least-squares method which weights all data equally, and derives the bond values giving the best overall fit with the data. The results of this analysis are compared in Table 3 with the bond values deduced in Tables 1 and 2. Although precise numerical agreement could not be anticipated, the correlations reveal no major discrepancy between the results of the empirical and the computer analyses, and the computer data confirm that the bonds *bca*/*dca* for acetates and *bc*/*dc* for acetamides are those of variable sign.

Conclusion.—Considerable difficulties have been experienced in attempting to relate the geometry and chiroptical properties of carboxy- and related compounds. No single semiempirical regional 'rule' has so far been shown to be adequate, and the limits within which a particular rule operates are not clearly understood.

The empirical mapping of the bonds around a chromophore as suggested in this paper may help to define more clearly the positions of the nodal surface involved for each geometrical situation for these and other

[12] D. M. Glick and H. Hirschmann, *J. Org. Chem.*, 1962, **27**, 3212.

TABLE 3

Contributions of bonds to total $\Delta\varepsilon$ in acetates and acetamides

The positions of the bonds with respect to the chromophore are shown in the Figure; bonds with the first code letter *b* or *d* lie in front of, or behind, the carboxy-group, respectively

Bond	$(\Delta\varepsilon)$OAc *	$(\Delta\varepsilon)$NAc *	Bond	$(\Delta\varepsilon)$OAc *	$(\Delta\varepsilon)$NAc *
ba	−0·40 (−0·43)	−1·4 (−0·99)	*da*	+0·40 (+0·43)	+1·4 (+0·99)
bc	−0·20 (−0·12)	*either* −0·20 (+0·03) *or* +0·80 (+0·92)	*dc*	+0·20 (+0·12)	*either* +0·20 (−0·03) *or* −0·80 (−0·92)
bd	−0·50 (−0·57)	−0·20 (−0·28)	*db*	+0·50 (+0·57)	+0·20 (+0·28)
bab	−0·10 (−0·11)	−0·50 (−0·65)	*dad*	+0·10 (+0·11)	+0·50 (+0·65)
bac	−0·15 (−0·01)	−0·60 (−0·44)	*dac*	+0·15 (+0·01)	+0·60 (+0·44)
bca	*either* −0·20 (−0·15) *or* +0·20 (+0·14)	+1·60 (+1·87)	*dca*	*either* +0·20 (+0·15) *or* −0·20 (−0·14)	−1·60 (−1·87)
bcb	0·0 (+0·05)	+0·10 (−0·31)	*dcd*	0·0 (−0·05)	−0·10 (+0·31)
bda	−0·70 (−0·55)	−3·90 (−3·71)	*dba*	+0·70 (+0·55)	+3·90 (+3·71)
bdc	−0·40 (−0·25)	−2·40 (−2·27)	*dbc*	+0·40 (+0·25)	+2·40 (+2·27)

* Values deduced by computer analysis are shown in parentheses.

chromophores, and also to establish which features of the molecule are of most significance in determining the observed c.d.

EXPERIMENTAL

C.d. curves were measured for methanolic solutions (*ca.* 1 mg ml^{-1}) with path lengths of 1—10 mm, on either a Jouan Dichrograph-185 or a Cary-61 recording spectropolarimeter.

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