743. *Optical Rotatory Dispersion. Part XIX.*[1] *A Series of Acids, Imidazolines, Amidinium Chlorides, and their Copper Complexes, Related to Mandelic Acid*

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The optical rotatory dispersion (o.r.d.) curves of a series of α-hydroxy-acids related to mandelic acid show that the Cotton-effect curves observed are generally due to the $n \longrightarrow \pi^*$ transition of the carboxyl group and not to the phenyl absorption band (260—280 mμ). The o.r.d. curves for the related amidinium chlorides show distinct extrema in the 250—280 mμ region when the phenyl group carries an alkoxy-substituent. The o.r.d. curves of the amidinium chlorides, however, are more complex than those of their parent acids and not so useful for configurational assignments. Copper complexes derived from these α-hydroxy-amidinium chlorides, show a Cotton effect at about 590 mμ. Compounds of D-configuration have a positive Cotton effect in this region. This rule has permitted the assignment of configuration to some ten amidines, not previously correlated by chemical means.

THE optical rotatory dispersion curves of mandelic acid and some related aromatic acids of known absolute configuration have been measured, together with those of some related amidinium chlorides. Curves for a few imidazolines and copper complexes of α-hydroxy-amidines have also been measured.

For purposes of comparison use is made of the convention whereby some compounds are considered as their enantiomers. Thus the capital letter, E, in the tables of o.r.d. results indicates that, in fact, the enantiomer of the compound was measured and the signs have been changed accordingly.

The results of the o.r.d. measurements for the series of acids, amidinium chlorides, and copper complexes are given in Tables 1—5. The absolute configurations are also given in these Tables. Where the configuration has been previously determined the appropriate reference is given; if on the other hand the configuration has been deduced by the comparison of the o.r.d. curve with the curves of compounds of known configuration this is likewise indicated.

TABLE 1

O.r.d. data for α-hydroxy-α-aryl acids and related acids (I); data given for acids of D- or *R*-configuration; rotations of acids at D-line (589 mμ) and at 546 mμ all negative (solvent: methanol)

		First extremum (trough)		Lowest wavelength reached		Ref. for absolute configuration
R	R′	[ϕ]	λ (mμ)	[ϕ]	λ (mμ)	
H	H	−20,700° *	232	0°!	222	*a*
Me	H	−10,020	230	−6000!	225(E) ‡	*b*
Et	H	−13,200	231	−6170!	225(E)	*c*
H	Me	−18,500	233	+14,600!	213	*d*
H	CO_2Me	−21,300	232	+16,100!	214(E)	*e*
H †	H(*o*-OMe)	−21,200	235	−7400!	230(E)	*e*

* Lit.,[2] +20,700° for (E), in 0·1N-HCl, at 231 mμ. † Optical purity unknown; other extrema (−2770tr, 276 mμ and −2460pk, 264 mμ) are presumably due to the aromatic chromophore. ‡ (E), measured as enantiometer.

[a] K. Mislow, *J. Amer. Chem. Soc.*, 1951, **73**, 3954. [b] J. H. Brewster, *J. Amer. Chem. Soc.*, 1956, **78**, 4061. [c] S. Mitsui, S. Imaizumi, Y. Senda, and K. Konno, *Chem. and Ind.*, 1964, 233. [d] A. McKenzie, *J.*, 1899, **75**, 753. [e] By comparison with curves of acids with known configurations.

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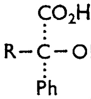
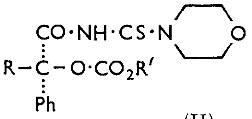
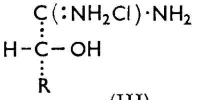
[1] Part XVIII, see J. R. Bull, J. P. Jennings, W. Klyne, G. D. Meakins, P. M. Scopes, and G. Snatzke, *J.*, 1965, 3152.

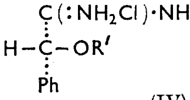
Acids.—Dirkx and Sixma [2] have recently shown that, for the D-α-hydroxy-acids (lactic, isopropyl-lactic, tartaric, and mandelic acids), the carboxyl group is associated with a negative Cotton effect in 0·1N-HCl. We have run, in methanol, a series of α-hydroxy-acids (I) related to mandelic acid. The o.r.d. results are given in Table 1 and confirm the findings of Dirkx and Sixma. With one possible exception the aromatic absorption band (260—280 mμ) does not appear to give a Cotton effect (this was also observed with phenylalanine [2]) and the Cotton-effect curves are related to the carboxyl $n \longrightarrow \pi^*$ absorption band at *ca.* 205 mμ. *o*-Methoxymandelic acid, however, shows a small inflexion in the o.r.d. curve and this may well be due to the methoxy-substituent causing the phenyl absorption band in this region to give a Cotton effect. This effect of alkoxy-substitution is also noticed in the case of the amidinium chlorides which are discussed later.

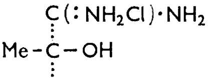
Other o.r.d. studies on aromatic chromophores have recently appeared—see T. M. Hooker and C. Tanford, *J. Amer. Chem. Soc.*, 1964, **86**, 4989; L. Verbit, *ibid.*, 1965, **87**, 1617; cf. also P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, 1965, for previous references.

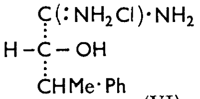

$$\begin{array}{c}\mathrm{CO_2H}\\ \vdots\\ \mathrm{R{-}C{-}OR'}\\ \vdots\\ \mathrm{Ph}\end{array}$$
(I)

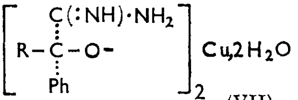

(II)

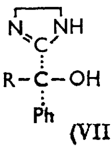

$$\begin{array}{c}\mathrm{C(\!:\!NH_2Cl){\cdot}NH_2}\\ \vdots\\ \mathrm{H{-}C{-}OH}\\ \vdots\\ \mathrm{R}\end{array}$$
(III)


$$\begin{array}{c}\mathrm{C(\!:\!NH_2Cl){\cdot}NH_2}\\ \vdots\\ \mathrm{H{-}C{-}OR'}\\ \vdots\\ \mathrm{Ph}\end{array}$$
(IV)


$$\begin{array}{c}\mathrm{C(\!:\!NH_2Cl){\cdot}NH_2}\\ \vdots\\ \mathrm{Me{-}C{-}OH}\\ \vdots\\ \mathrm{CH_2Ph}\end{array}$$
(V)


$$\begin{array}{c}\mathrm{C(\!:\!NH_2Cl){\cdot}NH_2}\\ \vdots\\ \mathrm{H{-}C{-}OH}\\ \vdots\\ \mathrm{CHMe{\cdot}Ph}\end{array}$$
(VI)


$$\left[\begin{array}{c}\mathrm{C(\!:\!NH){\cdot}NH_2}\\ \vdots\\ \mathrm{R{-}C{-}O^-}\\ \vdots\\ \mathrm{Ph}\end{array}\right]_2\mathrm{Cu,2H_2O}$$
(VII)


(VIII)

For purposes of comparison, the Cotton-effect curve of (+)-hydratropic acid (Ph•CHMe•CO_2H) was measured. The (+)-*S*-acid shows an extremum at 233 mμ, [φ] = +7830, which is further into the ultraviolet than was suggested by Sjöberg,[3] who, however, pointed out that his anomalous dispersion might not be real as he was working at the limit of the Rudolph instrument and hence again this Cotton effect appears to be based on the $n \longrightarrow \pi^*$ absorption band of the carboxyl group.

Full Cotton-effect curves may be obtained by the conversion of the acids into their

TABLE 2

O.r.d. data of morpholinothiocarbamide derivatives (II); all acids have the D- or *R*-configuration, and have negative rotations at D-line and at 546 mμ; all were measured as enantiomers except for the first compound listed

			First extremum (peak)		Second extremum (trough)		Amplitude	Ref. for absolute
R	R′	Solvent	[φ]	λ (mμ)	[φ]	λ (mμ)	*a*	configuration
H	Me	MeOH	+2720°	366	−7500°	303	+102	*a*
		Hexane	+7250	364	−12,100	313	+194	
Me	Me	MeOH	+3330	366	−10,070	309	+134	*b*
		Hexane	+5700	364	−13,830	303	+195	
Me	Et	MeOH	+3480	367	−8750	308	+122	*b*
		Hexane	+3750	362	−14,950	301	+187	
Et	Me	MeOH	+2770	366	−8365	306	+111	*c*
		Hexane	+6650	367	−13,900	318	+206	
Et	Et	MeOH	+2920	362	−9270	303	+122	*c*
		Hexane	+7985	366	−16,050	315	+240	

[a] K. Mislow, *J. Amer. Chem. Soc.*, 1951, **73**, 3954. [b] J. H. Brewster, *J. Amer. Chem. Soc.*, 1956, **78**, 4061. [c] S. Mitsui *et al.*, *Chem. and Ind.*, 1964, 233.

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[2] I. P. Dirkx and F. L. J. Sixma, *Rec. Trav. chim.*, 1964, **83**, 522.
[3] B. Sjöberg, *Acta Chem. Scand.*, 1960, **14**, 273.

TABLE 3

O.r.d. data of amidinium chlorides * [general formula (IV)] derived from mandelic and related acids; data given for amidinium chlorides having the D- or *R*-configuration; all compounds have negative rotations at 546 mμ.

Compound	R	R′	Substituents	Solvent	Extrema						Lowest wavelength reached		Ref. for absolute configuration
					[ϕ]	λ (mμ)	[ϕ]	λ (mμ)	[ϕ]	λ (mμ)	[ϕ]	λ (mμ)	
1	H	H	—	MeOH							−12,500°!	217	*a*
				Water					−2860° tr	233	−2680!	227	*a*
2	Me	H	—	MeOH			−1060° tr	250			+540!	227(E)	*b*
				Water			−320tr	250	+3650pk	222	+2830!	220(E)	*b*
3	Et	H	—	MeOH			−1080tr	244			−480!	232(E)	*c*
				MeOH			−1420tr	243			−1170!	234	*c*
				Water			−470tr	248	+1760pk	226	+1570!	222(E)	*c*
				Water			−840tr	246	+1170pk	222	0!	218	*c*
4	Me	H	*m*-Me	MeOH							−1290!	238	*d*
				Water			−860tr	259—244	+1390pk	223	0!	220	*d*
5	Me	H	*p*-Me	MeOH			−1130tr	256			−995!	244	*e*
				Water			−890tr	256	+1330pk	231	+900!	229	*e*
6	H	H	*p*-Me	MeOH							−2340!	247(E)	*f*
				Water							−2030!	236(E)	*f*
7	H	H	*o*-OMe	MeOH	−4360tr	280	−1690pk	261	−17,000tr	229	−15,100!	227	*g*
8	H	H	*o*-OEt	MeOH	−3910tr	283	−1450pk	258	−9450tr	234	−7900!	231(E)	*h*
9	H	H	*m*-OEt	MeOH	Fine structure	292—263	−4860tr	240			−3580!	237	*h*
10	H	H	*p*-OEt	MeOH	−1370tr	281	−320pk	260	−1770tr	246	0!	243(E)	*i*
11	H	H	*p*-OMe	MeOH	−2440tr	278	0pk	262			−1900!	245	*h*
12	H	H	*o*-Cl	MeOH					−18,950tr	225	−9250!	220(E)	*h*
				Water					−2490tr	227	0!	224(E)	*h*
13	H	H	*o*-Br	MeOH					−5600tr	231	−4830!	227(E)	*h*
				Water					−2230tr	233	+6250!	222(E)	*h*
14	H	H	3,4-(OMe)$_2$	MeOH			−4000tr	260	0pk	249	−2500!	240	*h*
15	H	H	2,3-(OMe)$_2$	MeOH	−2260tr	280—270	−1140 to 1480sh	265—244			−590!	235(E)	*h*
16	H	H	2,4-Cl$_2$	MeOH							−5300!	233	*h*
				Water					−2910tr	238	−2760!	236	*h*
17	H	Me	—	MeOH					−6950tr	227	−6300!	222(E)	*j*

[a] S. Reid, Ph.D. Thesis, St. Andrews, 1949. [b] R. Roger and D. G. Neilson, *J.*, 1959, 688. [c] R. Roger and D. G. Neilson, *J.*, 1961, 3181. [d] Curve of compound No. 4 in water is very similar to the curves of Nos. 2 and 3 in water. [e] Curve of compound No. 5 in water is similar to the curves of Nos. 3 and 4 in water. [f] Tentative assignment on basis of negative curve. [g] Curve of compound No. 7 is very similar to the curves of No. 8. [h] From curves of copper complexes (cf. Table 5). [i] Curve of compound No. 10 is similar to the curve of No. 11. [j] D. G. Neilson and D. A. V. Peters, *J.*, 1963, 4455.

* For methods of preparation see references in the text.

morpholinothiocarbamide derivatives [4] (II) and the results for a few acids are presented in Table 2. All the (—)-acids have positive curves, and this is further evidence for the configurations assigned to the acids in Table 1.

Amidinium Chlorides.—Table 3 shows the major extrema observed in o.r.d. measurements of amidinium chlorides derived from mandelic and related acids. The amidinium chlorides give irregular results in water; the first extremum of the Cotton effect, when it can be reached, is at about 220 mμ, corresponding probably to an absorption band for the $H_2N{\cdot}C{\vdots}NH_2{}^+$ group at 190—200 mμ, although this region is complicated by the presence of phenyl absorption. Curves measured in methanol show similar tendencies but water is to be preferred as it is more transparent in the 220-mμ region.

Some of the curves of the amidinium chlorides listed in Table 3 are not so definitely positive or negative as those of the acids (see Figure 1), and for the purpose of assignment of configuration the chemical evidence (*viz.*, hydrolysis) is in some cases preferable to the o.r.d. evidence (cf. refs. in Table 3). For the majority of compounds described in Table 3, it seems reasonable, from a comparison with curves of compounds of known configuration, to assign the D- or *R*-configuration to those amidinium chlorides which have negative curves. Where the aromatic ring in these amidines bears an alkoxy-substituent, the o.r.d. curves increase in complexity and extrema occur in the 250—280 mμ region. As the u.v. spectrum of this region for the series [5] of aliphatic α-hydroxyamidinium chlorides (III; R = Me, Et, Pr^n, or Pr^i) is featureless, these extrema must be attributed to optically active aromatic absorption bands.

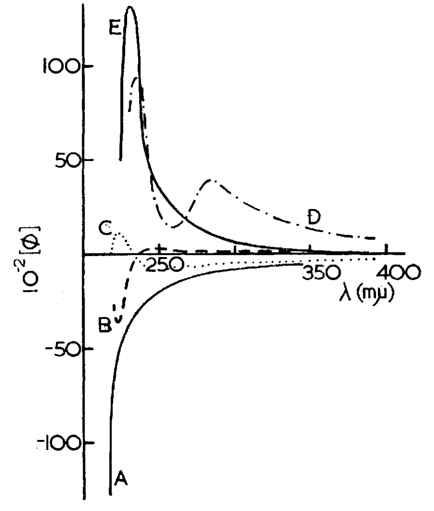

FIGURE 1. O.r.d. curves

A, (—)-Mandelamidinium chloride (in methanol). B, (+)-Atrolactamidinium chloride (in water). C, (—)-α-Hydroxy-α-phenylbutyramidinium chloride (in water). D, (+)-*o*-Ethoxymandelamidinium chloride (in methanol). E, (+)-α-Hydroxy-α-phenylbutyric acid (in methanol).

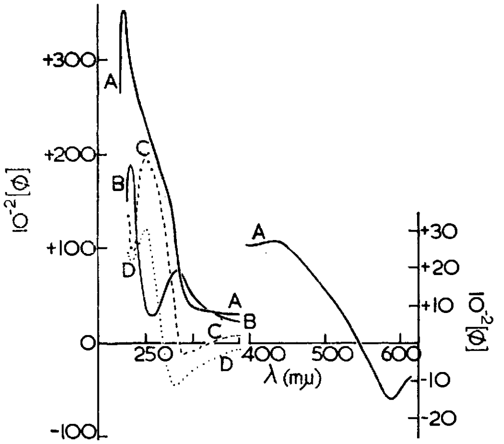

FIGURE 2. O.r.d. curves (solvent: methanol)

A, Copper complex of (—)-*o*-ethoxymandelamidinium chloride (recorded as its enantiomer). B, 2 × (+)-*o*-Ethoxymandelamidinium chloride. C, Difference curve (A — B). D, Difference curve for 2 × (+)-*o*-bromomandelamidinium chloride and its copper complex.

The compounds of Table 4, lactamidinium chloride and two β-aryl-substituted derivatives, are not directly comparable with the larger group in Table 3 in which the aryl group is in the α-position. It is apparent that the introduction of a phenyl group into the

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[4] C. Djerassi, K. Undheim, and A. Weidler, *Acta Chem. Scand.*, 1962, **16**, 1147.

[5] D. A. V. Peters, Ph.D. Thesis, University of St. Andrews, 1963.

TABLE 4

O.R.D. data of miscellaneous amidinium chlorides; all have negative rotations at 546 mμ

Compound	Solvent	Extremum (trough)		Lowest wavelength reached		Absolute configuration	Ref.
		$[\phi]$	λ (mμ) .	$[\phi]$	λ (mμ)		
(III; R = Me)	MeOH			−1330°!	217	L	*a*
	Water			−1290!	216		
(V)	MeOH	−17,100°	215	−14,700!	212	D	(E) *b*
	Water	−10,400	220	−6620!	213		
(VI)	MeOH	−22,800	214	−12,800!	212		*c*
	Water	−10,800	217	−8800!	213		

[a] D. G. Neilson and D. A. V. Peters, *J.*, 1962, 1309. [b] D. G. Neilson and D. Ewing, *J.*, 1965, 770. [c] Configuration unknown but o.r.d. curve compares well with that for (V); compound (VI) is therefore probably D at the α-hydroxy-centre; cf. R. Roger and D. G. Neilson, *J.*, 1961, 3181.

lactamidinium system, either in the α- or β-positions, causes a reversal of sign of rotation for compounds of related configuration. Unfortunately no Cotton effect was observed for lactamidinium chloride above 217 mμ although it is likely, from the plain curve obtained (cf. Table 4), to be positive for the D-isomer. Similar behaviour due to phenyl substitution in acylthioureas of α-substituted alkylcarboxylic acids has been discussed by Djerassi *et al.*[4]

Complexes with Copper(II).[6]—Pfeiffer and Christeleit [7] showed that the copper complexes of α-amino-acids had anomalous rotatory dispersions in the visible region and that these could be used for the correlation of configuration of the parent acids. Similar correlations have also been obtained using the copper salts of certain α-hydroxy-acids.[8]

As it was known that the α-hydroxy-amidines were capable of forming complexes with transition metals and in particular that the copper complexes had a broad absorption band of low extinction coefficient ($\varepsilon < 50$) in the visible region,[9,10] it was thought that the complexes derived from optically active α-hydroxy-amidines might prove useful in assigning configurations to those amidines which could not be correlated by chemical means.[11]

It was found that the o.r.d. curves of the copper(II) complexes (VII) of the α-hydroxy-amidines [6] do show significant features in the regions of 590 and 220 mμ, and that a few have extrema at 270 mμ (cf. Table 5).

The sign of the Cotton effect at *ca.* 590 mμ is positive for complexes derived from the D- or *R*-series of amidines and negative for the L-series, thus affording a useful method for the determination of the absolute configuration of the amidines, particularly since the measurement of the o.r.d. of the parent compounds does not always give a clear answer to their configuration.

It is of interest to note that the amino-acids which have an " inverse " system to that of the α-hydroxy-amidines, *i.e.*, a terminal acidic group and a basic α-grouping, give copper complexes which show a positive Cotton-effect curve in this region for the L-series.[7]

The feature at 270 mμ can probably be ascribed to a $d \longrightarrow d$ transition of copper.[10] At first sight the behaviour in this region ($\sim$270 mμ) appears more complex than at the longer wavelengths, the 2-chloro-, 2-bromo-, and 2,4-dichloro-mandelamidine copper complexes all showing distinct extrema which appear to be absent in the case of, *e.g.*, the 2- or 3-ethoxy- or 4-methoxy-mandelamidine copper complexes. However, in these latter compounds, the amidine ligands themselves exhibit Cotton-effect curves in this region (cf. Table 3) and these are in the opposite sense to those derived from the copper transition. By contrast, the halogen-substituted ligands are featureless in this region.

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[6] L. H. Roach and D. G. Neilson, previous Paper.

[7] P. Pfeiffer and W. Christeleit, *Z. physiol. Chem.*, 1937, **245**, 197; **247**, 262.

[8] P. Karrer and J. Heyer, *Helv. Chim. Acta*, 1937, **20**, 407.

[9] R. O. Gould, R. F. Jameson, and D. G. Neilson, *Proc. Chem. Soc.*, 1960, 314.

[10] R. O. Gould and R. F. Jameson, *J.*, 1963, 15.

[11] D. G. Neilson and D. A. V. Peters, *J.*, 1963, 4455.

TABLE 5

O.r.d. data of copper complexes of amidines having the general formula (VII); data given for complexes formed from amidinium chlorides having negative rotations at 546 mμ and the D- or *R*-configuration (solvent: methanol)

R	Substituents	Extremum (peak)		Extremum (broad shoulder or trough)		Extremum (peak)		Extremum (trough)		Extremum		Lowest wave-length reached		Ref. for absolute configuration of the amidinium chloride
		[φ]	λ (mμ)	[φ]	λ (mμ)	[φ]	λ (mμ)	[φ]	λ (mμ)	[φ]	λ (mμ)	[φ]	λ (mμ)	
H *	—	+2320°	588	−2420° to −3680°	483—300			−24,600°	245	−16,900° pk	234	−20,200° !	227	*a*
Me	—	+620	588	−1450 to −1650	450—313							−15,750 !	242	*b*
Et	—	+830	595	−1780 to −1960	460—312							−23,200 !	235	*c*
H	*o*-OMe	+780	589	−1950 to −2200	472—400							−35,200 !	227	*d*
H	*o*-OEt	+1500	591	−2700 to −3860	442—300					−35,200tr	226	−26,800 !	223	*d*
H	*o*-Cl	+1600	598	−1640	467	+51,500°	278	−15,900	240	−11,000pk	233	−37,500 !	225	*d*
H	*o*-Br	+2000	585	−1340	455	+2540	282	−16,800sh	252—244	−29,000tr	224	−25,200 !	220(E)	*d*
H	*p*-OMe	+1080	585	−2420 to −2480	457—330			−14,500	251			−8750 !	240(E)	*d*
H	*p*-OEt	+1280	589	−2080 to −1610	459—311			−15,200	253			−10,700 !	242(E)	*d*
H	*m*-OEt	+1860	585	−3240 to −3440	420—313							−29,700 !	236	*d*
H	2,4-Cl_2	+2120	580	−1290	461	+8600	283					−32,400 !	230(E)	*d*
Complex of (V)		+415	581	−700 to −340	459—317							−17,600 !	227	*d*

* This first complex contains 0—$2H_2O$, so molecular rotations quoted could be up to 10% too high.

[a] S. Reid, Ph.D. Thesis, St. Andrews, 1949. [b] R. Roger and D. G. Neilson, *J.*, 1959, 688. [c] R. Roger and D. G. Neilson, *J.*, 1961, 3181. [d] Deduced from sign of C.E. at 590 mμ.

TABLE 6

Ultraviolet absorption spectra of amidinium chlorides [general formula (IV; R′ = H)]

R	Substituents	Solvent	Absorption maxima λ (mμ) with log ε in parentheses						
H		MeOH		252(2·18)	258(2·33)	264(2·27)	267(2·07)		
		Water	191·5(4·94)						
Me		MeOH		253(2·18)	259(2·31)	265(2·25)	268·5(2·04)		
		Water	196(5·68)						
Me	*m*-Me	MeOH				261sh	267(2·65)	274(2·56)	
Me	*p*-Me	MeOH		222sh (3·93)	257(2·33)	263(2·37)	269(2·25)		
H	*p*-Me	MeOH		223sh (3·92)	257(2·34)	264·5(2·36)	269(2·24)		
H	*o*-Me	MeOH		220sh?				277(3·29)	
H	*o*-OEt	MeOH		220sh?				277(3·78)	
		Water	191—194(5·11)						
H	*m*-OMe	MeOH		~224sh (3·71)					278—285(3·25)
H	*m*-OEt	MeOH		~230sh (3·74)				278(3·31)—285	
		Water	189(4·93)						
H	*p*-OMe	MeOH		234·5(3·95)				275·5(3·11)	281·5(3·04)
		Water	~192(4·80) *						
H	*p*-OEt	MeOH		234·5(3·99)				276·5(3·09)	282·5(3·00)
		Water	196(5·43)						
H	2,3-$(OMe)_2$	MeOH							282·5(3·29)
H	*o*-Cl	MeOH				263·5(2·90)	268·5(3·00)	276(2·89)	
H	*o*-Br	MeOH			259·5(2·45)	265·5(2·53)		272·5(2·39)	
		Water	198(4·65) *						
H	2,4-Cl_2	MeOH		220sh?		263(2·31)		273(2·40)	281·5(2·27)
Acetamidinium chloride		Water	199(4·96)	Featureless in the region: 250—280 mμ					
Lactamidinium chloride (III; R = Me)		Water	194(4·42)	Featureless in the region: 250—280 mμ					
α-Benzyl-lactamidinium chloride (V)		MeOH		253(2·12)	259(2·24)	265(2·14)			

* Spectra recorded on a Unicam S.P. 700.

Accordingly, difference curves representing the o.r.d. curve of the copper complex minus twice the o.r.d. curve of the amidinium chloride were plotted (Figure 2) and show clearly the 270-mμ feature as a positive Cotton effect in those complexes derived from the D-series of amidinium chlorides. The mandelamidinium copper complex does not show the extremum on the difference curve, but analysis points to this complex being slightly different from the others.[6,10]

The copper complex of lactamidine [12] could not be obtained as a solid and was prepared and used *in situ*; [6] the D-amidine complex was associated with a positive Cotton effect in the 580-mμ region, as in the preceding cases.

Imidazolines.—The o.r.d. curves of mandelo-, atrolacto-, and α-hydroxy-α-phenylbutyro-imidazolines were recorded first as the free base (VIII) in methanol and then as the protonated base prepared by the addition of a few drops of concentrated hydrochloric acid to the methanolic solution. In the range studied (400—250 mμ) all gave plain curves with a molecular rotation less than 1000° at 300 mμ. There is a positive shift in rotation on protonation of the imidazole nucleus when the configuration at the α-hydroxy-centre is known [13,14] to be L, *e.g.*, in the atrolactic system, and this has been used by Neilson and Ewing[14] to assign tentatively the L-configuration to (+)-2-(α-benzyl-α-hydroxyethyl)-imidazoline, its (+)-amidinium chloride, and its hydrolysis product (+)-α-benzyl-lactic acid. This assignment is now confirmed by the sign of the Cotton-effect curve of the copper complex derived from the amidine (cf. Table 5). Such behaviour closely parallels that very recently described by Dirkx and de Boer [15] for the closely related ephedrines, the o.r.d. curves of which, on changing the solvent from ethanol to 0·1N-HCl, show a positive shift for these compounds with an α-L-configuration. Unfortunately it has not proved possible to obtain the optically active amidines from their hydrochlorides and hence no comparable results on the effect of protonation are available for them.

EXPERIMENTAL

O.r.d. measurements were made at 20—25° with the Bellingham and Stanley/Bendix-Ericsson spectropolarimeter "Polarmatic 62." Concentrations were in the range 0·02—1 mg./ml. for most compounds.

Resolution of o-*Methoxymandelic Acid.*—Ethyl *o*-methoxymandelimidate hydrochloride [11] (50 g.) was dissolved in water and the resultant ester hydrolysed by sodium hydroxide solution. The crude (±)-acid (30 g.) so obtained was heated with ephedrine (25 g.) in ethanol (60 ml.) and set aside to crystallise at 0°. The resultant solid was recrystallised from the minimum of ethanol and then decomposed with dilute sulphuric acid to give (+)-*o*-methoxymandelic acid which, after crystallisation from benzene–cyclohexane, had $[\alpha]_{5461}^{20}$ +175·9° (*c* 0·52 in acetone) and m. p. 87—88°. The original liquors yielded, in the same way, the (−)-isomer, $[\alpha]_{5461}^{20}$ −168·0° (*c* 0·86 in acetone) and with m. p. 80—83°.

Resolution of Acids (*Table* 1).—These were prepared and resolved by the standard literature methods. The mandelic acids [16] had $[\alpha]_{5461}^{20}$ ±185° (in acetone) and their *O*-methyl derivatives [17] had $[\alpha]_{5461}^{20}$ ±173° (in ethanol). The *O*-methoxycarbonyl derivative had $[\alpha]_{5461}^{20}$ +145·0° (in acetone),[18] and was prepared from (+)-mandelic acid, which had $[\alpha]_{5461}^{20}$ +182°. (±)-Atrolactic acid was resolved by the method of McKenzie and Clough [19] and had $[\alpha]_D$ +51·5° (in water). (±)-α-Hydroxy-α-phenylbutyric acid was resolved by the method of McKenzie and Ritchie [20] and had $[\alpha]_{5461}$ +35·0° (in water).

(−)-Hydratropic acid [21] had $[\alpha]_{5461}^{19}$ −113° (in benzene). All these values are in reasonable agreement with those quoted in the references.

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Morpholinothiocarbamide Alkyloxycarbonyl Derivatives.—The alkyloxycarbonyl derivatives (Table 7) were prepared from the relevant α-hydroxy-acid by interaction with methyl or ethyl chloroformate.[18] The alkyloxycarbonyl derivative was then converted into its morpholinothiocarbamide by the method of Djerassi, Undheim, and Weidler.[4] The infrared peaks at 5·88 μ and the ultraviolet maxima at ~286 and ~345 mμ are characteristic of this class of compound. All compounds in Table 7 gave a peak in the i.r. spectrum at 5·88 μ.

TABLE 7

Morpholinothiocarbamide alkyloxycarbonyl derivatives (II)

Sign of parent acid	R	R′	M. p.	$\lambda_{max.}$ (mμ)	log ε	Found (%) C	Found (%) H	Required (%) C	Required (%) H
−	H	Me	126—127°	286	4·06				
				345	2·38				
+	Me	Me	160—161	285	4·08				
				345	2·46				
+	Me	Et	156—157	286	4·14	56·0	6·3	55·7	6·0
				345	2·47				
+	Et	Me	134—135	286	4·12				
				344	2·49				
+	Et	Et	166—167	286	4·14	56·7	6·6	56·8	6·3
				345	2·49				

Amidines and Imidazolines. These were prepared and resolved by the literature methods[5,11-14,22,23] and were in good agreement with the literature values unless otherwise stated.

Copper(II) *Complexes of α-Hydroxy-amidines.*—The preparation of these complexes is described by Neilson and Roach.[6]

Ultraviolet Spectra.—The u.v. spectra of the amidinium chlorides were measured over the 220—320-mμ range in methanol on an Optica CF4R spectrophotometer. The u.v. spectra in the 195—220-mμ range were measured in water under nitrogen on a Hilger and Watts Uvispek spectrophotometer (cf. Table 6).

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