

N-Quaternary Compounds**Part XXIII. Optical Rotatory Dispersion and Circular Dichroism****Studies of Pyridinium Analogues of α -Amino Acids**

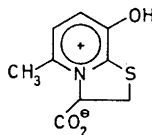
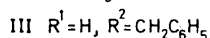
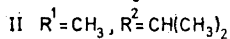
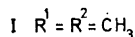
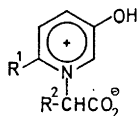
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ORD and CD curves have been recorded for α -3-hydroxypyridinium carboxylic acids. The acids investigated had the L-configuration and gave Cotton effect with negative CD maxima in the 300–350 m μ region and Cotton effect with CD maxima in the 215–240 m μ region in both acid and alkaline solution. The higher wavelength maxima are associated with the pyridyl chromophore and the lower wavelength maxima arise from the carboxyl and pyridyl chromophores. Both Cotton effects undergo a red shift on changing from acid to alkaline solution.

The ORD and CD properties of α -amino acids have been extensively studied.^{1,2} We now wish to report ORD and CD curves for hydroxypyridinium analogues of α -amino acids. The spectra were recorded in 0.1 N HCl and 0.1 N NaOH. In acid solution both the carboxylic acid and the phenolic groups will be undissociated while both groups are dissociated in alkaline solution.

The carboxyl group in amino acids is the chromophore with the highest wavelength absorption band, the $n \rightarrow \pi^*$ transition of which occurs at about 205–210 m μ . L-Amino acids exhibit a positive Cotton effect in acid or neutral solution with an ORD peak in the 215 m μ region and a CD maximum at about



IV

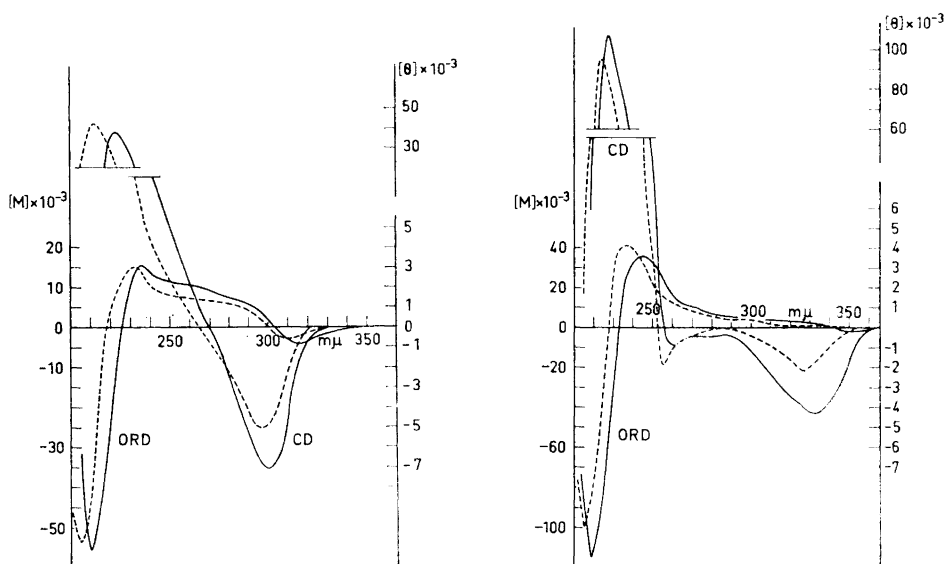


Fig. 1. ORD and CD curves for I (---) and II (—) recorded in 0.1 N HCl.

Fig. 2. ORD and CD curves for I (---) and II (—) recorded in 0.1 N NaOH.

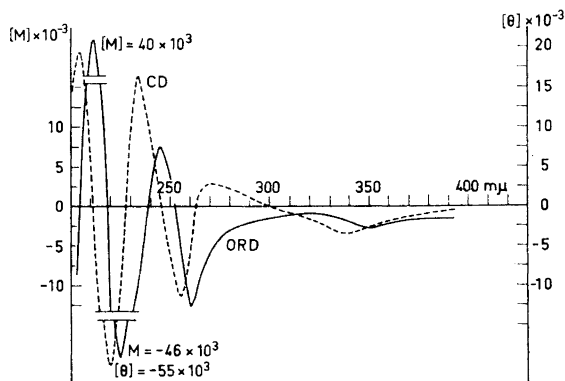


Fig. 3. ORD and CD curves for IV recorded in 0.1 N HCl.

210 $m\mu$ attributed to the carboxyl chromophore.^{2,3} Protonation of the amino group moves the absorption to shorter wavelengths. A hypsochromic shift is also found for the ionization of the carboxyl group.³

Our findings are simplest discussed in terms of the alanine (I) and valine (II) analogues. In both cases it was possible to record the ORD and CD curves down to nearly 200 $m\mu$.

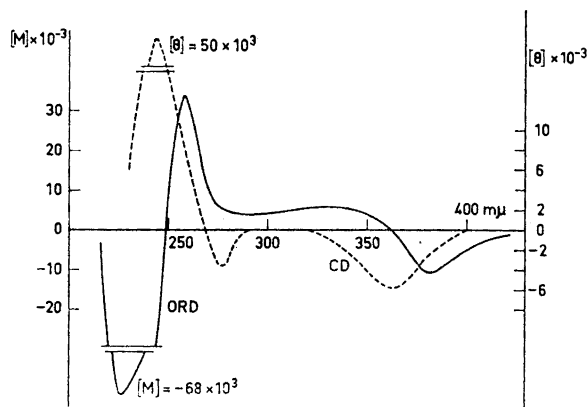


Fig. 4. ORD and CD curves for IV recorded in 0.1 N NaOH.

The observed CD maxima in acid solution for the pyridinium-alanine (I) and pyridinium-valine (II) analogues are at 213 and 221 $m\mu$, respectively, while the corresponding amino acids in acid solution have this maximum at 209 $m\mu$. In NaOH the CD maxima are found at even higher wavelengths *viz.*, at 223 and 228 $m\mu$, respectively.

These L- α -pyridinium acids thus exhibit a positive Cotton effect around 220 $m\mu$ in HCl which is shifted 5–10 $m\mu$ towards longer wavelengths in NaOH. Thus in contrast to the behaviour of amino acids the shift in alkali in the pyridinium analogues is bathochromic. The opposite wavelength shift must arise from interaction between the carboxyl and pyridyl chromophores which both are directly attached to the chiral carbon. A such interaction could also explain that the absorption occurs at higher wavelength than in simple amino acids.

The pyridyl group also gives rise to extrema in polarized light at higher wavelengths. Thus the CD curve for the alanine analogue (I) in HCl has a negative maximum at 298 $m\mu$ and the valine analogue (II) at 300 $m\mu$. These absorptions in NaOH are moved to 327 and 333 $m\mu$, respectively, in agreement with the respective phenol-phenolate UV shift from 300 to 332 $m\mu$ and 302 to 334 $m\mu$.⁴ The UV spectra in NaOH also show a pyridyl absorption band at 244–250 $m\mu$ which is optically active with CD maxima for I and II at 255 and 261 $m\mu$ respectively. This transition is not apparent from the ORD curves. It will be noticed that the negative Cotton effects attributed to the pyridinium chromophore at the highest wavelength have reduced amplitudes compared to the positive Cotton effect of the carboxyl–pyridinium chromophores in the 220 $m\mu$ region.

The curve for the phenylalanine analogue (III) in HCl exhibits similar positive and negative maxima at 225 and 294 $m\mu$, respectively. In addition a multiple Cotton effect is present at 260–270 $m\mu$ presumably due to the phenyl group acting as a β -chromophore. Similar β -chromophore effects near 275 $m\mu$ have been observed for tryptophane and tyrosine.⁵ In NaOH III shows the

expected negative CD maximum moved to 320 $m\mu$ while the multiple Cotton effect of the β -chromophore has not been moved. The CD curve has a negative maximum at 245 $m\mu$ and a negative minimum at 231 $m\mu$ but strong absorption prevented recording of the curve below about 220 $m\mu$. The ORD curve has a peak at 235 $m\mu$ with a trough at 215 $m\mu$.

The curves for the dihydrothiazolo[3,2-a]pyridinium derivative (IV) in NaOH resemble the curves from I and II but are shifted towards higher wavelengths. The carboxyl Cotton effect is presumably hidden by a stronger pyridine band with maximum at 246 $m\mu$. The negative CD maximum at 275 $m\mu$ must be due to the pyridinium ring corresponding to the 255–261 bands in I and II. In HCl the curves could be recorded at the lower wavelengths. Both the negative Cotton effect with CD maximum at 340 $m\mu$ and the positive CD maximum at 243 $m\mu$ must arise through the pyridyl-chromophore. The positive and negative CD maxima at 268 $m\mu$ and 255 $m\mu$, respectively, must in some way be associated with the sulphur in the thiazolo ring acting as a β -chromophore. The thiazolo ring causes a bathochromic shift of the UV absorption bands. This shift could explain the appearance of a new ORD peak at 211 $m\mu$ with a CD maximum at 204 $m\mu$. Another strong CD maximum occurs at 218 $m\mu$ with negative sign. If the 204 $m\mu$ extremum were associated with the carboxyl chromophore, extrapolation into the inaccessible region for the monocyclic pyridinium derivatives (I–III) should give CD maxima for the carboxyl group (I–III) in the region of 180–190 $m\mu$ which seems unlikely. Therefore the CD maximum at 204 $m\mu$ must be associated with the pyridyl chromophore and the carboxyl chromophore is presumably associated with the 218 $m\mu$ maximum.

The spectra of a few more simple analogues have also been recorded and the Cotton effect curves are as described above. Thus it appears that Cotton effect curves for pyridyl carboxylic acids of the above type should be of value for structural and stereochemical studies.⁶

EXPERIMENTAL

The pyridinium acids were prepared from L-amino acids.^{4,7,8} Because of optical instability, due to the activation by the quaternary nitrogen, the compounds I–III are partially racemized. The samples of I and II studied had $[\alpha]_D + 14^\circ$ (c 0.8 in N HCl) and $[\alpha]_D + 79^\circ$ (c 0.8 in N HCl), respectively. Data for III, not presented graphically, are given in full below. Compound IV is believed to be optically pure and data are therefore given in full.

The ORD and CD measurements were made on a Cary model 60 spectropolarimeter.

The spectra were recorded in 0.1 N HCl aq. and 0.1 N NaOH aq.: $C = 2 \times 10^{-3}$ mol/10 ml; temperature 27°; the cell length was 1 mm.

I.-2-(3-Hydroxypyridinium)-3-phenylpropionate (III).

	$[\alpha]_D = -82^\circ$	(c 0.4 in 0.1 N HCl).
CD in 0.1 N HCl:	$[\theta]_{294} - 4.700$, $[\theta]_{277} - 3.500$, $[\theta]_{270} - 4.200$, $[\theta]_{266} - 3.400$, $[\theta]_{263} - 4.000$, $[\theta]_{242} 0$, $[\theta]_{234} + 6.800$.	
in 0.1 N NaOH:	$[\theta]_{360} - 3.100$, $[\theta]_{296} 0$, $[\theta]_{268} - 3.500$, $[\theta]_{266} - 2.700$, $[\theta]_{263} - 4.200$, $[\theta]_{260} - 3.500$, $[\theta]_{246} - 7.900$, $[\theta]_{231} - 3.300$.	
ORD in 0.1 N HCl:	$[\phi]_{305} - 4.700^\circ$, $[\phi]_{280} - 300^\circ$ (inflection), $[\phi]_{268} + 1.100^\circ$, $[\phi]_{265} + 900^\circ$, $[\phi]_{262} + 1.900^\circ$, $[\phi]_{258} + 1.800^\circ$, $[\phi]_{242} + 7.600^\circ$, $[\phi]_{213} - 27.600^\circ$.	

ORD in 0.1 N NaOH: $[\phi]_{343} - 3.300^\circ$, $[\phi]_{310} + 600^\circ$, $[\phi]_{272} - 4.500^\circ$, $[\phi]_{268} - 3.200^\circ$,
 $[\phi]_{264} - 4.100^\circ$, $[\phi]_{257} - 3.000^\circ$, $[\phi]_{252} - 4.000^\circ$, $[\phi]_{235} + 3.200^\circ$,
 $[\phi]_{215} - 3.800^\circ$, $[\phi]_{208} + 11.000^\circ$.

L-8-Hydroxy-5-methyldihydrothiazolo[3,2-a]pyridinium-3-carboxylate (IV)

$[\alpha]_D = -132^\circ$ (c 0.6 in 0.1 N NaOH).
 CD in 0.1 N HCl: $[\theta]_{340} - 3.000$, $[\theta]_{300} 0$, $[\theta]_{268} + 3.000$, $[\theta]_{262} 0$, $[\theta]_{255} - 11.500$,
 $[\theta]_{245} 0$, $[\theta]_{234} + 16.500$, $[\theta]_{226} 0$, $[\theta]_{218} - 55.000$, $[\theta]_{210} 0$,
 $[\theta]_{204} + 24.000$.
 in 0.1 N NaOH: $[\theta]_{360} - 5.800$, $[\theta]_{320} 0$, $[\theta]_{290} 0$, $[\theta]_{275} - 4.500$, $[\theta]_{268} 0$,
 $[\theta]_{247} + 50.000$.
 ORD in 0.1 N HCl: $[\phi]_{345} - 2.300^\circ$, $[\phi]_{315} - 1.000^\circ$ (broad), $[\phi]_{260} - 12.400^\circ$,
 $[\phi]_{244} + 7.500^\circ$, $[\phi]_{223} - 46.000^\circ$, $[\phi]_{211} + 40.000^\circ$.
 in 0.1 N NaOH: $[\phi]_{382} - 10.800^\circ$, $[\phi]_{335} + 5.500^\circ$ (broad), $[\phi]_{290} + 4.200^\circ$ (broad),
 $[\phi]_{258} + 34.000^\circ$, $[\phi]_{225} - 68.000^\circ$.

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