Absolute Configuration at C-2 of Some Necic Acids

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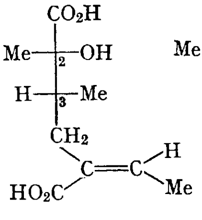
THE chemical structures of almost all the known necic acids have been elucidated,[1] but the absolute configuration has been determined only in the cases of senecic acid, its geometrical isomer integerrinecic acid, hydrophyllinecic, jaconecic, and isojaconecic acids, all of which have the same absolute configuration[2] (*R*) at C-2.

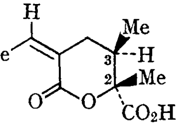
The absolute configuration of 2*R*,3*S*-(+)-senecic acid (I) has been determined by *X*-ray analysis.[3] The acid forms very easily the corresponding lactone (II), which can be hydrogenated catalytically to give 2*R*,3*S*-(−)-dihydrosenecic acid lactone (III).

The use of our method of asymmetric transformation and, independently, the comparison of o.r.d. curves for determining the absolute configuration of senecic acid gave correct results in both cases. We have used both methods for determining the absolute configuration at C-2 of some other necic acids. The results obtained by using the latter method are reported here.

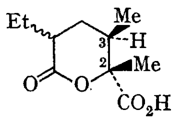
The u.v. spectra of five- and six-membered-ring lactones exhibit absorption maxima at about 220 nm. Because of high absorption below 220 nm., we were not able to measure the complete Cotton effect corresponding to this optically active absorption band, but only the first extremum.



(I)



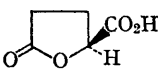
(II)



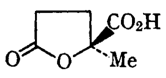
(III)

The o.r.d. curves of *S*-(−)-γ-butyrolactone-γ-carboxylic acid (water) (IV), the absolute configuration of which has been established by correlation with *R*-(+)-glyceraldehyde, and *S*-(−)-γ-valerolactone-γ-carboxylic acid (water) (V) exhibit positive Cotton effects; those of acids with the reverse configuration exhibit a negative one.

It is to be expected, therefore, that five- and six-membered-ring lactone-acids with the carboxyl group on the carbon atom immediately bound to the heterocyclic oxygen atom, o.r.d. curves of which exhibit positive Cotton effects, have the

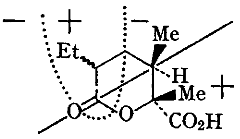


(IV)



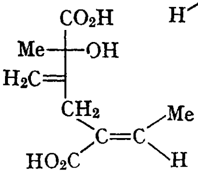
(V)

S-configuration at this carbon atom and *vice versa*. This assumption is supported by the o.r.d. curve of 2*R*,3*S*-dihydrosenecic acid (III), which exhibits a negative Cotton effect. The sign of the Cotton effect is also in accordance with the octant rule adapted to six-membered-ring lactones[4] [the rotatory increment of the carboxyl group at C-2 is more important than that of the methyl group, *cf*. (VI)].

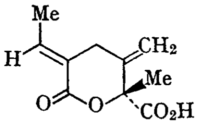


(VI)

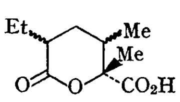
2*R*-(—)-Seneciphyllic acid (VII) (originally called α-longinecic acid) has a structure similar to that of senecic acid.[5] The absolute configuration of its centre of chirality has not previously been established. The acid very easily forms the lactone (VIII), which can be hydrogenated to 2*R*-(—)-tetrahydroseneciphyllic acid lactone (IX).



(VII)



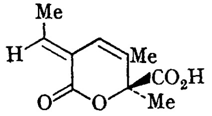
(VIII)



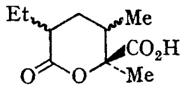
(IX)

A negative Cotton effect has been observed in the o.r.d. curve of the acid (IX), indicating the same absolute configuration in acids (IX) and (III). (—)-Seneciphyllic acid (VII) has, therefore, the same absolute configuration as senecic acid at the corresponding chiral centre.

S-(—)-Clivonecic acid (X) formed by hydrolysis of alkaloid clivorine, has a similar structure.[6] Catalytic hydrogenation of the acid gives 2*S*-(+)-tetrahydroclivonecic acid (XI).



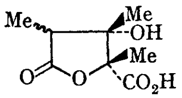
(X)



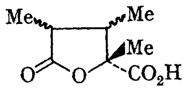
(XI)

The o.r.d. curve of clivonecic acid exhibits a minimum at 262 nm., $[\Phi]_{\text{min}}$ — 12,600° and a maximum at 230 nm., $[\Phi]_{\text{max}}$ + 40,800° (methanol). A positive Cotton effect in the o.r.d. curve of the acid (XI) indicates the *S*-configuration for tetrahydroclivonecic acid and, consequently, to clivonecic acid. The sign of the observed Cotton effect is again in agreement with the modified octant rule.

2*R*,3*S*-(—)-Monocrotalic acid (XII) serves as an example of five-membered-ring lactone-acid. Its structure and the relative configuration at C-2 and C-3 have been determined by synthesis.[7] The acid can be converted into 2*R*-(+)-dihydroanhydromonocrotalic acid (XIII) in several steps.



(XII)



(XIII)

The o.r.d. curves of both acids as well as that of *R*-(+)-γ-valerolactone-γ-carboxylic acid exhibit

TABLE

Compound	λ_{max} (nm.)	$[\phi]_{\text{max}}$ (MeOH) (deg.)	Absolute configuration at C-2
(III)	235	−2420	*R*
(IV)	232	+ 448	*S*
(V)	234	+1710	*S*
(IX)	237	− 920	*R*
(XI)	237	+1050	*S*
(XII)	234	−3360	*R*
(XIII)	234	−1090	*R*

negative Cotton effects, which suggests the absolute configuration at C-2 of both acids as being *R*. From the known relative configuration the *S*-configuration at C-3 of monocrotalic acid follows. The absolute configuration at the third centre of chirality of monocrotalic acid remains as yet unknown.

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