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ON THE STEREOCHEMISTRY OF CORONATINE : REVISED ABSOLUTE CONFIGURATION OF (+)-CORONAMIC ACID

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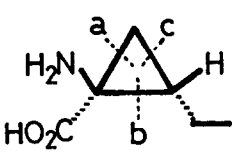
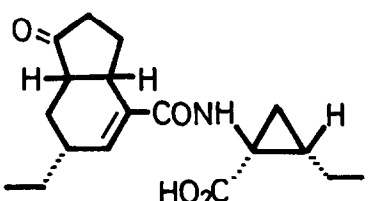
In the previous paper, we reported the stereochemistry of coronatine[1], in which amino acid part, (+)-coronamic acid, was described as the enantiomer of 1 on the basis of application of sector rule.[2] In this communication, we would like to describe further investigation on the stereochemistry of coronamic acid, and we are forced to conclude that the absolute configuration should be revised as 1 by the enzymatic method[3] and X-ray analysis, and total stereostructure of coronatine must be depicted as 2.



1



2

It was expected that if (+)-coronamic acid has a stereochemistry 1, and is hydrogenolized by catalytic hydrogenation, D-isoleucine and L-alloisoleucine

will be resulted through cleavage of cyclopropane ring (a). In the experiment, hydrogenolysis of 1 over 10% Pd-C under pressure of 14 kg/cm^2 at 80° induced cleavages at all three bonds (a, b and c) of the cyclopropane ring and afforded four amino acids, isoleucine, alloisoleucine, norleucine, and 2-amino-2-methylvaleric acid, whose structures were identified by PMR spectra and amino acid analyser (elution time 3.69, 3.58, 3.91, 3.57 hr). When the reaction products were treated with L-amino acid oxidase (Crotalus adamanteus, Carbiochem.), only the peak (3.58) ascribing to alloisoleucine was decreased in amino acid analyser. On the other hand, treatment of the reaction products with D-amino acid oxidase (hog kidney, Tokyo Kasei) resulted to decrease isoleucine. These observations indicate that the alloisoleucine and isoleucine have L- and D-configuration respectively, and the stereochemistry of their precursor, (+)-coronamic acid, should be represented to be (+)-(1S,2S)-1-amino-2-ethylcyclopropanecarboxylic acid (1), which is reversal of sector rule.[1] The results of the same treatments on (-)-coronamic acid and (+)-allocoronamic acid[4] are summarized in Table 1.

Table 1. Absolute configuration of (+)-coronamic acid and the stereoisomers deduced from enzymatic oxidation

Hydrogenolized amino acid	products	Amino acid oxidized with		absolute configuration
		L-amino acid oxidase	D-amino acid oxidase	
(+)-coronamic acid	Ile	AlloIle	Ile	(1S, 2S)
(-)-coronamic acid	AlloIle	Ileu	AlloIle	(1R, 2R)
(+)-Allocoronamic acid	NorLeu AMVA	AlloIle	Ile	(1R, 2S)

Abbreviation : Ile = isoleucine, AlloIle = alloisoleucine,
NorLeu = norleucine, AMVA = 2-amino-2-methylvaleric acid

From these results, stereochemistries of these amino acids were determined to be (-)-(1R,2R)-1-amino-2-ethylcyclopropanecarboxylic acid and (+)-(1R,2S)-1-amino-2-ethylcyclopropanecarboxylic acid, respectively. The absolute configuration of (-)-coronamic acid was further confirmed by X-ray analysis of its N-acetate. The crystal data are as follows: $C_8H_{13}NO_3$, orthorhombic, space group $P2_12_12_1$, a = 11.858(3), b = 13.928(3), c = 5.572(2), A, Z = 4, D_c = 1.236 $g \cdot cm^{-3}$. Intensity data for $2\theta < 140^\circ$ were collected on an automatic, four-circle diffractometer using Cu Kα radiation monochromatized with an LiF crystal. 1023 unique structure factor amplitudes greater than their estimated standard deviations were used for the structure determination. The structure was solved by the Monte Carlo direct method[5] on the basis of 218 E-values above 1.30. An E-map computed with 217 phases revealed the locations of all 12 independent non-hydrogen atoms. After 13 hydrogen atoms had been located in a difference Fourier map, several cycles of the full-matrix least-squares refinement were

Table 2. Bijvoet inequalities

h	k	l	$\overline{F}_o$ a)	$\overline{F}_c$ b)	ΔF_o c)	ΔF_c d)	h	k	l	$\overline{F}_o$	$\overline{F}_c$	ΔF_o	ΔF_c
3	2	1	4.69	3.80	0.08(2)	-0.11	3	6	1	8.65	8.54	0.09(2)	-0.10
1	12	3	4.69	4.92	0.17(3)	-0.09	8	5	2	5.19	5.08	-0.02(3)	0.06
10	5	1	5.90	6.03	0.12(3)	-0.10	8	1	1	4.69	4.73	0.06(3)	0.06
7	8	1	4.56	4.99	0.05(3)	-0.07	10	3	4	6.05	5.97	-0.05(3)	0.07
3	5	1	5.89	5.51	-0.16(2)	0.07	5	2	2	4.93	4.64	-0.01(3)	-0.05
6	6	3	7.77	8.09	0.10(3)	-0.12	4	6	5	5.85	5.59	0.09(3)	-0.06
4	4	6	5.25	5.56	-0.04(3)	0.08	2	6	1	4.86	5.12	0.07(2)	-0.06
6	7	1	5.02	4.92	0.05(3)	-0.07	4	9	3	7.44	7.64	0.09(3)	-0.09
7	4	3	4.90	4.68	0.03(3)	-0.07	6	2	4	8.95	9.73	0.13(3)	-0.11
8	3	2	6.24	6.60	0.15(3)	-0.08	4	4	2	9.12	8.54	0.38(2)	-0.08

a) $\overline{F}_o = \{|F_o(hkl)| + |F_o(h\bar{k}l)|\}/2$ b) $\overline{F}_c = \{|F_c(hkl)| + |F_c(h\bar{k}l)|\}/2$

c) $\Delta F_o = |F_o(hkl)| - |F_o(h\bar{k}l)|$ The e.s.d.'s for ΔF_o's are given in parentheses

d) $\Delta F_c = |F_c(hkl)| - |F_c(h\bar{k}l)|$

carried out including these hydrogen atoms. The R-value reached 5.9%. For the application of the Bijvoet method[6], out of the reflections with $|F_o| > 4.5$, 20 pairs of hkl and $h\bar{k}l$ reflections having the greatest values of $|F_c(hkl)| - |F_c(h\bar{k}l)| \,/\, \{|F_c(hkl) + F_c(h\bar{k}l)|\}$ were selected. The results are summarized in Table 2. The observed values for ΔF's were corrected for the absorption effect according to the Engel method.[7] This table clearly indicates that the actual absolute configuration of N-acetyl-(-)-coronamic acid corresponds to that shown in Fig. 1.

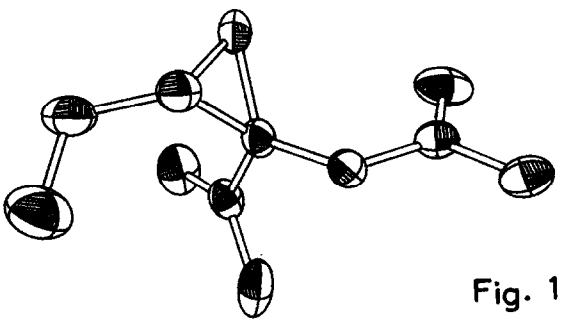


Fig. 1

References and footnotes

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