Hydrolysis of 3-Methyl-2-*n*-propylthio-4(3*H*)-quinazolinone (II)——6N Hydrochloric acid (15 ml) was added to a solution of 3-methyl-2-*n*-propylthio-4(3*H*)-quinazolinone (2.34 g) in absolute ethanol (30 ml) and the resulting solution was heated under reflux for 4 hr. Distilled off ethanol and poured the reaction mixture into ice-cold water. White needles separated which were filtered and dried. Recrystallization of this from ethanol gave 1.5 g of pure 3-methyl-2,4-(1*H*,3*H*)-quinazolindione (III), mp 244° (Found: C, 61.32; H, 4.49; N, 15.80. $C_9H_8N_2O_2$ requires: C, 61.37; H, 4.54; N, 15.92%).

The above filtrate gave characteristic reactions of the mercaptans and the mercaptan was identified to be *n*-propyl mercaptan as usual.

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Studies on Cerulenin. VI.[1] Some Spectroscopic Features of Cerulenin

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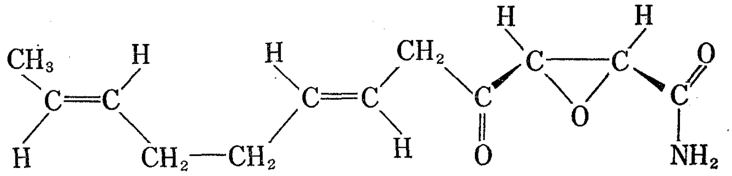
The structure of antifungal antibiotic, cerulenin[3] has been reported in the previous paper[1] as (2*S*) (3*R*)-2,3-epoxy-4-oxo-6,10-dodecadienoyl amide (see Fig. 1).



(2*S*) (3*R*) 2,3-epoxy-4-oxo-6,10-dodecadienoylamide
Fig. 1. Cerulenin

However, the configurations of the two double bonds in the structure were not completely determined. It became clear that, of the two double bonds in cerulenin, one had a *trans* configuration from the strong absorption (–CH out-of-plane bending)[4] at 967 cm^{-1}, which disappeared when cerulenin was converted into the tetrahydride.[1] In general, when the chemical shifts for two protons in the olefinic region in the nuclear magnetic resonance (NMR) spectrum are different, the *cis* and *trans* configuration can be distinguishable by the coupling constant values between the two protons. In cerulenin, the coupling constant values and the configuration of olefinic proton could not be determined because four olefinic protons were equal magnetically. Later, from the results of investigation of NMR spectra of cerulenin and related compounds it has been found that

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[1] Part V: S. Ōmura, M. Katagiri, A. Nakagawa, Y. Sano, S. Nomura, and T. Hata, *J. Antibiotics, Ser. A*, **20**, 349 (1967).
[2] Location: *Shirokane, Minato-ku, Tokyo.*
[3] T. Hata, Y. Sano, A. Matsumae, Y. Kamio, S. Nomura, and R. Sugawara Abstr. 33rd Annual Meeting of the Japan Bacteriological Society, Japan, *J. Bacteriol.*, **15** (10), 1075 (1960).
[4] R.R. Hampton, *Anal. Chem.*, **21** (8), 923 (1949).

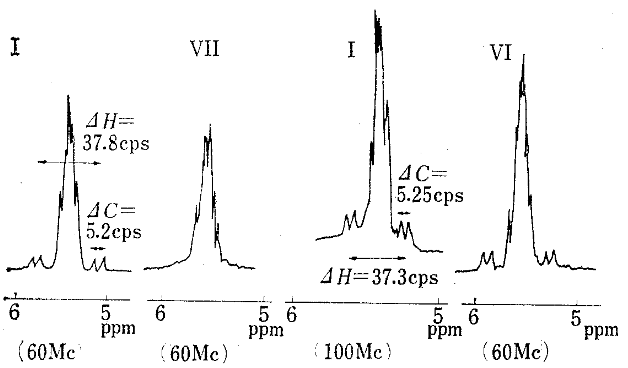

Fig. 2. NMR Spectra of I, VI, and VII

the double bond at C–10 has a *trans* configuration. In the present paper, some interesting data on the solvent effect of cerulenin on NMR spectrum and on circular dichroism (CD) curve are reported. The NMR spectrum of cerulenin in carbon tetrachloride exhibits an absorption at 5.45 ppm due to olefinic protons, but symmetric side bands are observed on both sides accompanying main absorption of olefinic protons (see Fig. 2). The ΔC values and the ΔH values of doublet of the both side absorptions are shown in Table I.

Table I. NMR (60 Mc) Data of Olefinic Protons of Cerulenin and Its Related Compounds

Compounds	bp °C/mmHg (mp °C)	NMR of olefinic proton		
		δ (ppm)	ΔH (cps)	ΔC (cps)
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2\text{-}C_8H_{10}O_3N\end{smallmatrix}$ (I)[1]	(93—94)	*ca.* 5.45	37.8	5.2
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2\text{-}C_8H_{10}O_3N\end{smallmatrix}$ (I)[1]		*ca.* 5.45[a]	37.3[a]	5.25[a]
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_3\end{smallmatrix}$ (II)[b]		*ca.* 5.5		
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}CH_3\\H\end{smallmatrix}$ (III)[c]		*ca.* 5.5		
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2CH_3\end{smallmatrix}$ (IV)[d]		*ca.* 5.5	37.7	4.9
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}CH_2CH_3\\H\end{smallmatrix}$ (V)[e]		*ca.* 5.5		
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2OH\end{smallmatrix}$ (VI)[f]	31.3—33.2/11	*ca.* 5.5	37.6	5.1
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}CH_2OH\\H\end{smallmatrix}$ (VII)[g]	88 —89 /60	*ca.* 5.5		
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2CH_2COOH\end{smallmatrix}$ (VIII)[h]	98 —100/12	*ca.* 5.5	37.5	5.1
Elaidic acid (IX)[i]		*ca.* 5.5		
Oleic acid (X)[j]		*ca.* 5.5		

a) 100 Mc
b), c), d), e), f), g) the compounds (II), (III), (IV), (V), (IX), and (X) were purchased commerically.
h) R.F. Nystrom and W.G. Brown, *J. Am. Chem. Soc.*, **69**, 1197 (1947)
i) L.F. Hatch and S.S. Nesbitt, *J. Am. Chem. Soc.*, **72**, 727 (1950)
j) N.L. Drake and R.W. Reimenchneider, *J. Am. Chem. Soc.*, **52**, 5005 (1930)

It become apparent that the both side absorptions are characteristic only in the compounds which have a partial structure of $\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2\text{-}\end{smallmatrix}$ type such as pentene-2 (IV), crotyl alcohol (VI), or 2-hexanoic acid (VIII). From the fact that the both side absorptions were observed in olefinic proton of cerulenin, the double bond at C-10 position was found to be the *trans* form of $\begin{smallmatrix}CH_3\\H\end{smallmatrix}{>}C{=}C{<}\begin{smallmatrix}H\\CH_2\text{-}\end{smallmatrix}$ type. However, the both side absorptions in olefinic proton were not observed in the structure having two methyl groups or one methylene group, and also for *cis* form. Such a side absorptions were not shown in the tetrahydride.[1] The double bond at C–6 position in the cerulenin structure seemed to be in a *trans* configuration from the fact that the characteristic absorption at about 700 cm^{-1} region assigned to *cis* form in the infrared (IR) spectrum[4] was not observed when cerulenin was converted into its tetrahydride.[1] Absorption pattern of the proton adjacent to a carbonyl group in NMR spectrum is known to change by a magnetic anisotropic effect, because a carbonyl group forms a collision complex with a solvent molecule.[5] When cerulenin was measured in a mixed solution of deuterochloroform and benzene the remarkable change in the absorption for the protons at C–2, C–3, and C–5 positions was observed.[1] In the present case, it was noted that the pattern of the protons of epoxy group at C–2 and C–3 positions changed with changes in the proportion of deuterochloroform and benzene. As shown in Fig. 3, the absorption for two protons in the proportional ratio of benzene deuterochloroform=3:7 (v/v) appeared as a singlet, while the absorption in equal ratio of the two solvents appeared as an AB quartet.

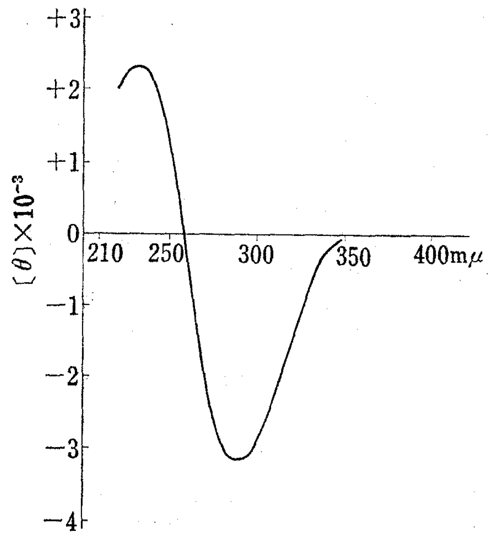

Fig. 4. CD Curve of Cerulenin in Dioxane

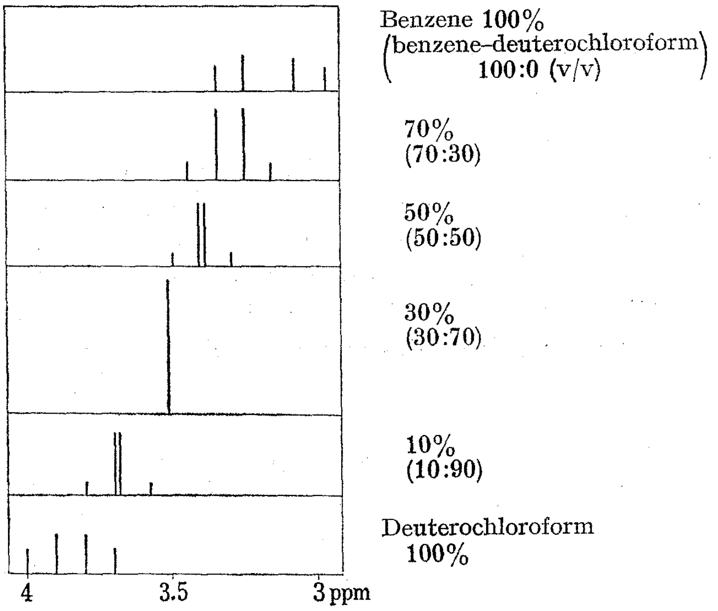

Fig. 3. Solvent Effect of Cerulenin in NMR Spectra (60 Mc)

Since the both carbonyl groups of cerulenin are joined to the optically active epoxide ring, n-π^* Cotton effect[6] is expected to appear, and the CD of cerulenin in dioxane was examined, by which two peaks, $[\theta]^{25}$ (mμ): −3138 (290) (negative maximum) and $[\theta]^{25}$ (mμ): +2320 (235) (positive maximum), were observed (see Fig. 4).[7]

The former is due to n-π^* Cotton effect of the carbonyl group of ketone adjoining the epoxide ring, and the latter is that of the acid amide. This is the first observation that the epoxide ring in a chain compound like cerulenin was found to contribute to the n-π^* Cotton effect of a carbonyl group.

When cerulenin was converted to dihydrocerulenin[1] to open the epoxide ring with chromous chloride, two main absorption bands, $[\theta]^{25}$ 290 mμ, $[\theta]^{25}$ 235 mμ for the epoxide ring on the CD curve disappeared completely.

Cerulenin in methanol was very unstable and consequently, antimicrobial activity decreased rapidly. This change is also revealed on the CD curve and the absorption at 290 mμ disappeared completely after 20 hours.

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[5] J. Ronayne and D.H. Williams, *Chem. Commun.*, **712** (1966).

[6] C.D. Jerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

[7] CD curves were taken with a JASCO ORD/UV-5 spectrometer.