

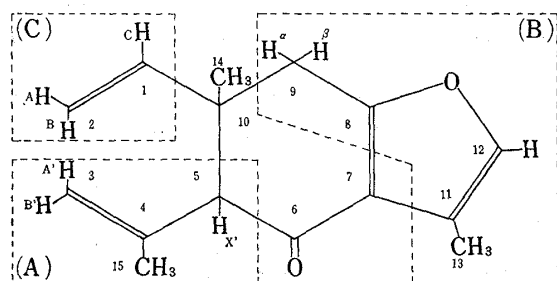
A Nuclear Magnetic Resonance Study of the Curzerenone¹⁾SHOGO UEMATSU, YUKIO AKAHORI, SEIGO FUKUSHIMA,
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The high-resolution proton magnetic resonance spectra of curzerenone observed in 20 mole percent solution in carbon tetrachloride and deuteriochloroform were analyzed with the aid of the computation and the double resonance experiments. The relative sign of the coupling constants was determined by the spin-tickling method, and the accurate values of parameters were obtained. It was confirmed the presence of the long-range spin coupling ${}^5J_{H-H}$ via the ether linkage in the fused furan ring, and the values of nuclear magnetic resonance parameters were shown to be reasonable for the predicted structure.

Introduction

From the rhizome of zedoary, *Curcuma zedoaria* ROSCOE (Zingiberaceae), a sesquiterpenoid compound, curzerenone, of the elemene type containing a fused furan ring was isolated, and the structure was elucidated by H. Hikino, *et al.*³⁾ and S. Fukushima, *et al.*⁴⁾ as shown in Chart 1.



curzerenone (I)

Chart 1

The nuclear magnetic resonance (NMR) spectrum showed fine structures, and the spectrum was analyzed in detail with the aid of computational experiments and double resonance experiments.

The accurate values of NMR parameters were obtained and the presence of the long-range spin coupling ${}^5J_{H-H}$ was confirmed and these NMR parameters were shown to be reasonable for the presumed structure (I). In this paper, the analysis of the spectrum is described as followings.

Experimental

Material—Curzerenone (I) was prepared by methods in the previous paper.⁴⁾

Solvents—Carbon tetrachloride, spectrograde, was purchased from Wako Pure Chemical Industries, LTD. Deuteriochloroform and tetramethylsilane from E. Merk AG. were used as solvent and internal reference, respectively.

Preparation of Samples—To the 20 mole% solution of curzerenone (I) in CCl_4 was added a suitable amount of tetramethylsilane, and the solution was degassed in NMR sample tube under vacuum 10^{-6} Torr by repeating freeze and thaw, then the tube was sealed. The $CDCl_3$ solution of I (20 mole%) was prepared by the same method.

- 1) A part of this work was presented at the 89 annual meeting of the Pharmaceutical Society of Japan, Nagoya, April, 1969.
- 2) Location: 2-2-1, Oshika, Shizuoka; a) Present address: National Institute of Hygienic Sciences, Setagaya-ku, Tokyo
- 3) H. Hikino, K. Agatsuma, and T. Takemoto, *Tetrahedron Letters*, 1968, 931; *idem, ibid.*, 1968, 2855.
- 4) S. Fukushima, M. Kuroyanagi, Y. Akahori, Y. Saiki, and A. Ueno, *Yakugaku Zasshi*, 88, 792 (1968).

Furthermore, the coupling of the proton at C-5 (173.6 Hz) with methylene protons at C-3 was observed and the coupling constants were found as 0.6 Hz for $J_{A'-5}$ and $J_{B'-5}$.

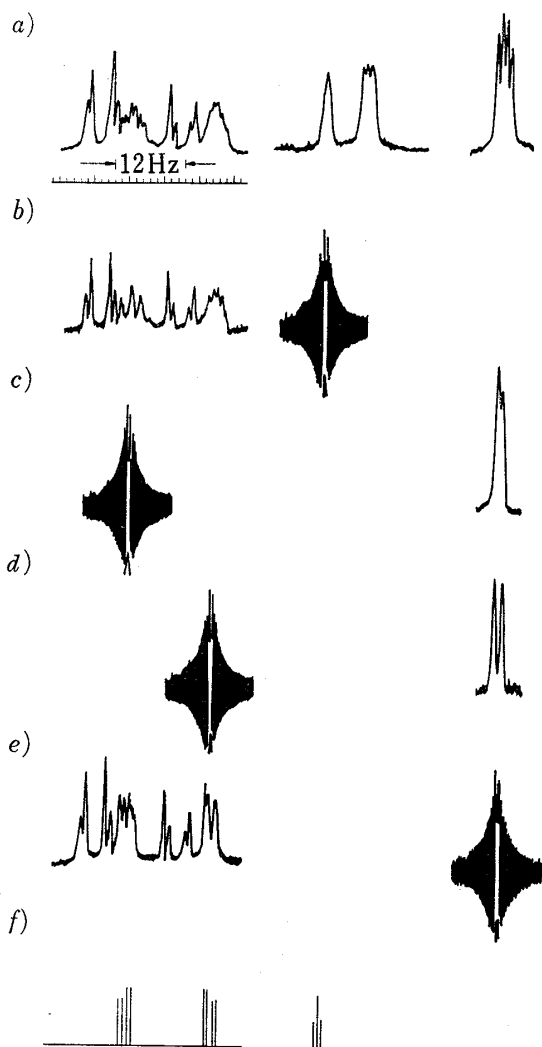


Fig. 2. NMR Spectrum of the Part Structure (A) of Curzerenone in CCl_4

a) is single-resonance spectrum for A.
b), *c*), *d*), and *e*) show double-resonance spectra with the 5-proton, a proton in the methylene group, the other proton in the methylene group, and the 15-methyl protons irradiated by strong r.f. field H_2 .
f) is calculated line spectrum for *e*).
 All the spectra are shown with the frequency increasing from right to left.

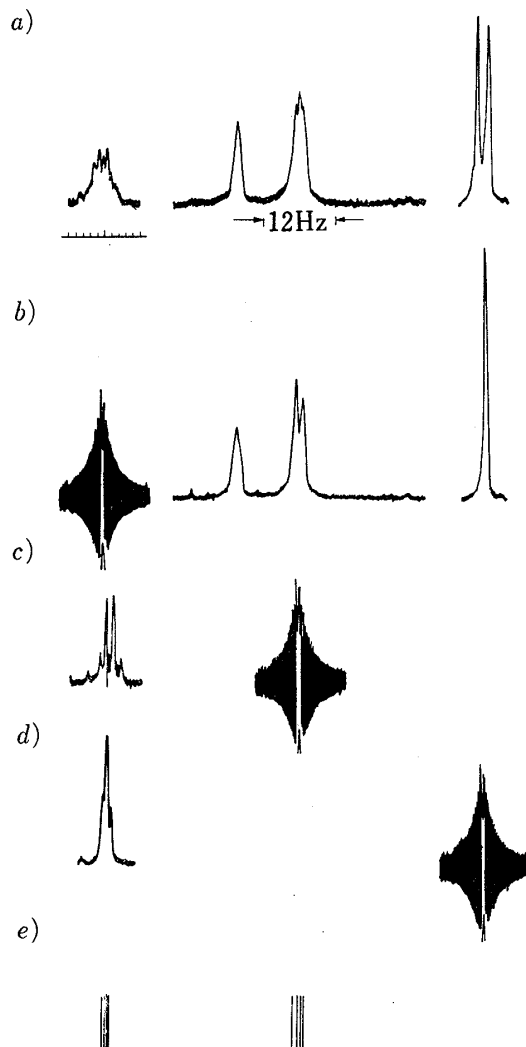


Fig. 3. NMR Spectrum of the Part Structure (B) of Curzerenone in CDCl_3

a) is single-resonance spectrum for B.
b), *c*), and *d*) show double-resonance spectra with the α -hydrogen on the furan ring, the 9-methylene protons, and the β -methyl protons irradiated by strong r.f. field H_2 .
e) is calculated line spectrum for *d*).
 All the spectra are shown with the frequency increasing from right to left.

The Analysis of ABM_3X System (Part Structure B)-Figure 3a

Irradiation on α -hydrogen on the furan ring at 424 Hz changed the methylene signals at C-9 into AB type signals and the β -methyl signals on the furan ring into a singlet as shown in Fig. 3b. Irradiation on C-9 methylene protons at 170 Hz transformed the signals of α -hydrogen into a quartet as shown in Fig. 3c. Irradiation on β -methyl protons at 130.5 Hz afforded a triplet of α -hydrogen as shown in Fig. 3d.

Therefore, it was concluded that α -hydrogen on the furan ring coupled with two protons (C-9 $_{\alpha}$, C-9 $_{\beta}$) and also with β -methyl protons, and that two protons (C-9 $_{\alpha}$, C-9 $_{\beta}$) showed geminal

coupling⁹⁾ because of magnetical nonequivalence. The coupling constants shown in Table III were determined by computer simulation.

The Analysis of ABC System (Part Structure C)-Figure 4a

The spectrum of three spin system of vinyl group was consisted of twelve lines, and three combination bands were not detected in this case. The transition numbers and assignment of the protons were shown in Fig. 4, the calculated line spectrum and energy diagram were given in Fig. 4 and Fig. 5. The calculation was carried out with iterative method, and the calculated line positions and intensities were in good agreement with the experimental values as shown in Table I. Though the relative sign of coupling constants was changed, the calcula-

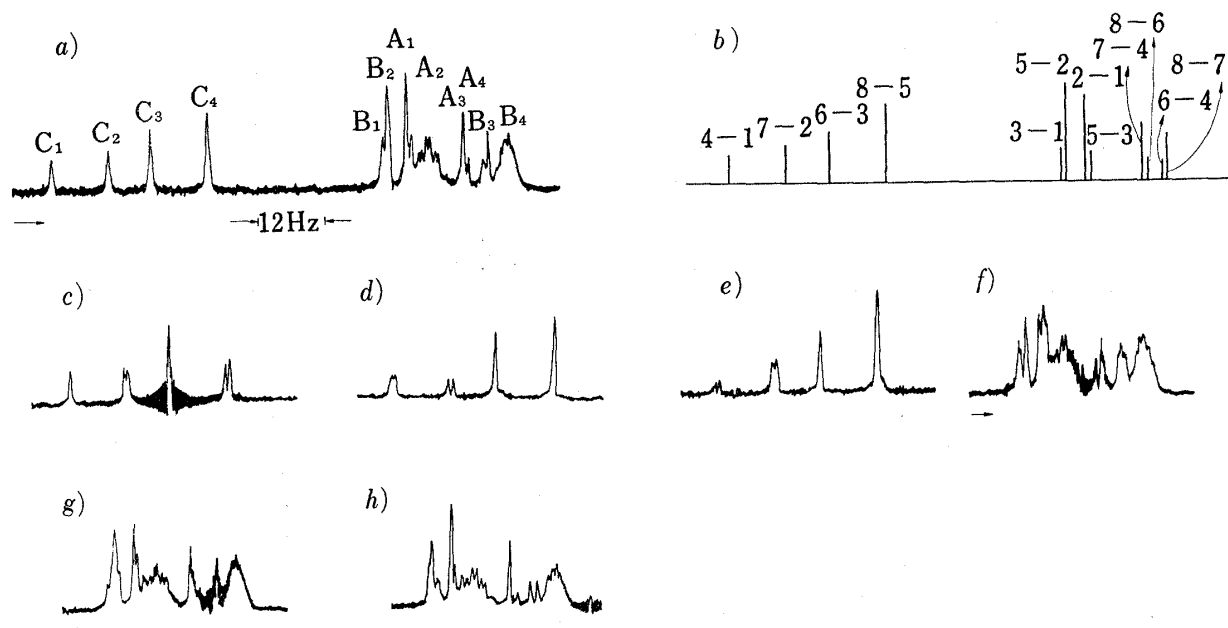


Fig. 4. NMR Spectrum of the Part Structure (C) of Curzerenone in CCl_4

a) is single-resonance spectrum for C.
 b) is calculated line spectrum for a).
 c), d), e), f), g), and h) show double-resonance spectra with line B_4 , line A_3 , line A_1 , line C_2 , line C_3 , and C_4 irradiated by weak r.f. field H_2 .
 All the spectra are shown with the frequency increasing from right to left.

ted spectral pattern did not afford marked change. Therefore, experimental method¹⁰⁾ was necessary for determination of the relative sign.

The relative sign in Table I and the corresponding energy level diagram shown in Fig. 5 were in agreement with the results of spin-tickling experiment as follows.

Irradiation at B_4 (transition 8—7) by weak *rf* field splitted the signal C_2 (transition 7—2) and C_4 (transition 8—5) into doublets as shown in Fig. 4c, and irradiation at A_3 (transition 7—4) afforded the same effect on signal C_1 (transition 4—1) and C_2 as shown in Fig. 4d. The similar results were shown in Fig. 4e,f,g, and h.

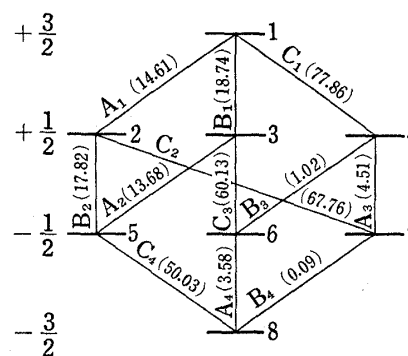


Fig. 5. NMR Energy Level Diagram for the Vinyl Protons of Curzerenone

9) K. Tori, 10th Symposium on The Chemistry of Natural Products, Symposium Papers, Tokyo, Oct. 6, 1966, p. 176.
 10) R. Freeman and W.A. Anderson, *J. Chem. Phys.*, **37**, 2053 (1962).

TABLE I. Final Values of $H, {}^a)J, {}^b)$ and the Comparison between Calculated Spectrum and Observed One (in CCl_4)

Iteration No. 10	$H_A=9.6967$ $J_{AB}=0.4709$	$H_B=10.8295$ $J_{AC}=10.8253$	$H_C=61.9487$ $J_{BC}=17.4538$		
transition	Obs. freq.	Calc. freq.	Difference	Calc. intensity	
5-4	—	-45.42494	—	0.000	
8-7	0.0	0.09997	-0.09997	0.946	
6-4	1.0	1.02500	-0.02500	0.381	
8-6	3.6	3.58748	0.01252	0.438	
7-4	4.5	4.51251	-0.01251	1.184	
5-3	13.7	13.68755	0.01245	0.614	
2-1	14.6	14.61244	-0.01244	1.760	
5-2	17.9	17.82506	0.07494	1.999	
3-1	18.8	18.74995	0.05005	0.673	
8-5	50.1	50.03742	0.06258	1.614	
6-3	60.2	60.13749	0.06251	1.057	
7-3	—	63.62500	—	0.001	
6-2	—	64.27500	—	0.000	
7-2	67.7	67.76251	-0.06251	0.760	
4-1	77.8	77.86244	-0.06244	0.566	

a) H is chemical shielding parameter (Hz).b) J is spin spin coupling constant (Hz).

TABLE II

Chemical shift (Hz)		Solvent CCl_4	Solvent CDCl_3
H_1	C	346.2	347.0
H_2	A	294.0	294.6
	B	295.2	296.2
H_3	A' (or B')	295.1	297.9
	B' (or A')	280.7	283.5
H_5	X'	173.6	180.3
H_9	α (or β)	170.3	173.6
	β (or α)	162.9	167.4
H_{12}		422.0	424.3
H_{13}		128.6	130.5
H_{14}		69.8	71.2
H_{15}		107.9	109.3

internal reference: TMS, concentration: ca. 20 mole percent

TABLE III

Coupling constant(Hz)	Solvent CCl_4	Solvent CDCl_3	Literature
J_{AB}	10.8	10.9	10.3 ¹¹⁾
J_{AC}	17.5	17.5	17.7 ¹¹⁾
J_{BC}	0.5	0.5	2.2 ¹¹⁾
$J_{A'B'}$	1.5	1.5	2.0 ⁸⁾
$J_{A'5}$ (or $B'5$)	0.6	0.6	
$J_{B'5}$ (or $A'5$)	0.6	0.6	
$J_{B'15}$ (or $A'15$)	1.4	1.1	-1.7 ⁸⁾
$J_{A'15}$ (or $B'15$)	0.7	0.6	-1.3 ⁸⁾
$J_{12,13}$	1.3	1.7	1.0—1.3 ⁹⁾
$J_{12,\alpha}$ (or $12,\beta$)	0.6	0.7	0.5—0.6 ⁹⁾
$J_{12,\beta}$ (or $12,\alpha$)	0.3	0.3	0.2 ⁹⁾
$J_{\alpha,\beta}$	17.5	17.8	15.0—15.3 ⁹⁾

11) Brügel, *Z. Elektrochem.*, **64**, 1121 (1960).

From these experiments the correct values of the chemical shifts and the coupling constants were obtained, and the values were shown in Table II, and III.

The obtained NMR parameters were reasonable for the structure of curzerenone.

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