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REVISION OF THE STRUCTURE OF A SESQUITERPENE FROM *LIGULARIA SAGITTA*

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Key Word Index—*Ligularia sagitta*; Compositae; sesquiterpene; revised structure; 2D NMR; X-ray diffraction.

Abstract—The structure of a new sesquiterpene from the rhizomes of *Ligularia sagitta* was revised as benzofuranoeremophil-1-ene by 2D NMR and X-ray diffraction.

INTRODUCTION

In a previous paper [1], we reported the isolation of a new sesquiterpene (**1**), mp 146–147°, $C_{15}H_{16}O$, from the rhizomes of *Ligularia sagitta*. It was reported to be benzofuranoeremophil-2-ene. A more recent 2D NMR study and an X-ray study have shown the compound to be benzofuranoeremophil-1-ene.

RESULTS AND DISCUSSION

The earlier NMR spectroscopic data established that compound **1** was a sesquiterpene, a three ring molecule with five double bonds. Since the benzofuran contained only four double bonds, the fifth one must be in the terminal six-member ring and was designated to be between C2 and C3 by means of ^1H and ^{13}C NMR spectra (Fig. 1). A more recent HETCOR spectrum shows the carbon atoms of the fifth double bond to be assigned at δ128.1 and 125.2 ppm, and their olefinic protons resonate at δ6.48 (*dd*, $J = 9.5$ and 3.3 Hz) and 5.88 (*ddd*, $J = 9.5$, 6.5 and 2.5 Hz), and the latter shows a connectivity with H-3β at δ2.24 (*dd*, $J = 17$ and 6.5 Hz) in the ^1H–^1H COSY spectrum. Meanwhile, the cross-peaks between H-3α at δ2.57(*m*) and H-4 at δ3.28 (*q*, $J = 7$ Hz), and H-4 and H-15 at δ1.09 (*d*, $J = 7$ Hz), were also observed. Thus, the analysis of the above 2D NMR spectral data proved the double bond is at C1/C2 rather than C2/C3.

The crystal structure of **1** was established by an X-ray diffraction study and is shown in Fig. 1. The positional coordinates and equivalent isotropic displacement coefficients for the non-hydrogen atoms of **1** are listed in Table 1. The study clearly establishes that the double bond is between C1 and C2 as the C1-C2 and C2-C3 bond lengths are 1.34(1) Å and 1.49(1) Å, respectively. The absolute configuration of C4 was determined as shown earlier [1, 2] and is as shown in Fig. 1.

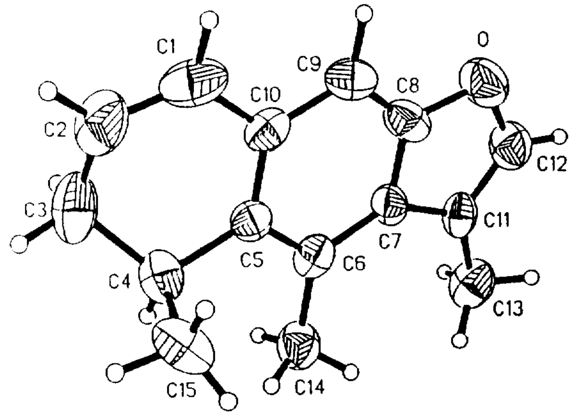

Fig. 1. A computer drawing of compound **1**. The figure gives the atom labels.

EXPERIMENTAL

NMR spectra. All NMR spectra (Table 1) were obtained with a Varian VXR-500 spectrometer equipped with a Sun 4/360 workstation. The sample was run at 26° in a 5 mm tube at a concn of 20 mg per 0.6 ml $CDCl_3$ with a trace of TMS as reference. In the COSY experiment, the f_1 and f_2 spectral width was 4 kHz, and the (t_1,

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t_2) data matrix was zero-filled to 2048 by 2048 to give a final resolution of 4 Hz per point. Sin-bell and Gaussian apodization were used in the f_1 and f_2 dimensions, respectively, to improve line shapes. For the HETCOR experiment, the spectral widths were typically 4 kHz in the f_1 (^{1}H) dimension and 20 kHz in f_2(^{13}C). The (t_1, t_2) data matrix was zero-filled to 1024 by 2048 to give a digital resolution of 8 Hz per point in the f_1 dimension and 20 Hz in the f_2 dimension. Processing was done using Gaussian apodization.

Crystal structure determination. A crystal of dimensions $0.10 \times 0.12 \times 0.46$ mm was mounted on a 4-circle diffractometer (Siemens R3m/V), which utilized graphite crystal monochromated Mo K_α ($\lambda = 0.71073$ Å) radiation. The lattice parameters and orientation matrix were determined using 26 carefully centred reflections ($9° \leqslant 2\theta \leqslant 25°$). The compound crystallizes in the orthorombic space group $P2_12_12_1$, with $a = 5.468(3)$, $b = 10.366(6)$, $c = 20.313(16)$ Å, $V = 1151.3(10)$ Å^3, $Z = 4$ and with a calculated density of 1.225 kg m^{-3}. The intensity data were collected at 20° using a variable speed (3.00–58.60° min^{-1}) 2θ–θ scanning procedures to a 2θ limit of 45°. The 2θ scan width for each reflection was from 1.20° before to 1.20° after the K_α separation. A total of 1243 reflections (1224 independent) were collected. Neither extinction nor absorption corrections were applied to the data. The absorption coefficient was 0.075 mm^{-1}. The crystal structure was solved using direct methods and refined using a full-matrix least-squares procedure. The positions of H atoms were calculated and a riding model was used in refinement process. A weighting scheme of the form $w^{-1} = \sigma^2(F) + 0.0011F^2$ was applied to the data set. The resulting R values were $R = 7.15\%$ and $R_w = 6.60\%$ with a goodness of fit of 1.14 for 700 observed reflections [$F > 2.5\sigma(F)$]. Atomic scattering factors were taken from ref. [3]. All programs used in the solution, refinement and display of this structure are included in a program package [4]. Supplementary materials including H positions, bond lengths and angles, and anisotropic thermal parameter are deposited at the Cambridge Crystallographic Data Centre.

Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients (Å$^2 \times 10^3$) for the non-hydrogen atoms of compound **1**

	x	y	z	U(eq)*
O	526(10)	832(5)	231(2)	57(2)
C(1)	1851(16)	−3683(8)	841(4)	61(3)
C(2)	871(19)	−4733(8)	1115(4)	66(4)
C(3)	−1525(17)	−4723(7)	1462(5)	69(4)
C(4)	−1874(14)	−3429(7)	1830(4)	46(3)
C(5)	−1323(13)	−2274(7)	1378(3)	37(2)
C(6)	−2544(15)	−1100(6)	1439(4)	41(3)
C(7)	−1847(13)	−86(7)	1021(3)	39(3)
C(8)	129(14)	−276(8)	591(4)	46(3)
C(9)	1352(14)	−1401(7)	528(4)	45(3)
C(10)	592(13)	−2431(7)	920(4)	42(3)
C(11)	−2619(14)	1237(6)	918(4)	39(3)
C(12)	−1182(16)	1712(7)	457(4)	53(3)
C(13)	−4679(14)	1962(6)	1240(4)	56(3)
C(14)	−4551(14)	−910(7)	1945(4)	50(3)
C(15)	−299(16)	−3327(7)	2443(4)	61(3)

*Equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.

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Table 2. ^{1}H and ^{13}C spectral data for compound **1** (500 MHz, CDCl$_3$, δppm)

No.	^{13}C	^{1}H	COSY
1	128.1	6.48 (*dd*, J = 9.5, 3.3 Hz)	5.88 (H-2)
2	125.2	5.88 (*ddd*, J = 9.5, 6.5, 2.5 Hz)	6.48 (H-1), 2.24 (H-3β)
3	31.1	2.24 (*dd*, J = 17, 6.5 Hz, H-3β)	5.88 (H-2), 2.57 (H-3α)
		2.57 (*m*, H-3α)	2.24 (H-3β), 3.28 (H-4)
4	27.5	3.28 (*q*, J = 7 Hz)	2.57 (H-3α), 1.09 (H-15)
5	127.8		
6	133.2		
7	130.0		
8	154.4		
9	107.4	6.98 (*s*)	
10	126.6		
11	116.5		
12	141.6	7.27 (*q*, J = 1 Hz)	
13	11.3	2.38 (*d*, J = 1 Hz)	
14	14.0	2.56 (*s*)	
15	19.5	1.09 (*d*, J = 7 Hz)	3.28 (H-4)