REVISED STRUCTURE OF RESORTHIOMYCIN

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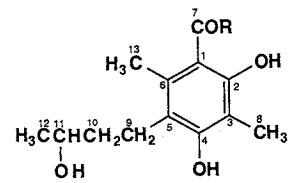
(Received for publication November 7, 1990)

Previously we reported the structure of a new antitumor antibiotic, resorthiomycin (**I**)[1] with an SCH_3 group at C-6 and an acetyl group at C-1 on the resorcinol nucleus (for numbering system, see Fig. 1). Based on the EI-MS and ^{13}C NMR data, Prof. HARUO SETO, University of Tokyo, suggested that the SCH_3 group should not directly bind to the benzene ring and, instead, forms a methylthio ester at C-1 carbon, since the mass spectral fragmentation peak $(M-SCH_3)^+$ of **I** and the long range ^{13}C-^1H couplings observed between a methyl proton and three carbons (C-1, C-5 and C-6) were not compatible with the proposed structure. Thus, we re-checked the position of the SCH_3 group by determining whether a methyl ester derivative (**II**) could be formed from resorthiomycin.

A mixture of resorthiomycin (2.5 mg) and sodium methoxide (4.8 mg) dissolved in dry MeOH (240 μl) was stirred overnight. The mixture was acidified with 50 mM HCl and extracted with ethyl acetate. The extract was purified by silica gel column chromatography developed with $CHCl_3$-MeOH (200:1) to yield 1.5 mg of **II**.

The FAB-MS of **II** revealed the molecular cluster ion peaks at *m/z* 291 $((M+Na)^+)$, 269 $((M+H)^+)$ and 268 (M^+). The ^1H NMR spectral data of **II** is shown in Table 1 in comparison of **I**, indicating that the signal of 14-CH_3 has shifted from 2.45 ppm to 3.93 ppm. This change suggests that the $-SCH_3$ group was replaced by an $-OCH_3$ group in **II**. The ^{13}C NMR spectrum of **II** in $CDCl_3$ revealed the following signals: δ_C 172.4, 160.0, 158.1, 136.8, 118.3, 109.6, 106.0, 66.7, 51.7, 37.5, 23.9, 21.9, 18.3 and 8.4. The signal of 7-C in **I** appeared at an extremely low field (198.2 ppm)[1], which is characteristic of the carbonyl carbon in a thio ester. In **II**, this signal has shifted to higher field (172.4 ppm), also suggesting the formation of an carboxylate.

Fig. 1. Structure of resorthiomycin (**I**) and its methyl ester derivative (**II**).



I (Resorthiomycin) R = $^{14}SCH_3$

II R = $^{14}OCH_3$

Table 1. Comparison of ^1H NMR spectral data between **I** and **II** (400 MHz, $CDCl_3$).

Proton	**I**		**II**	
	Chemical shift (ppm)	Multiplicity	Chemical shift (ppm)	Multiplicity
2-OH	9.80[a]	s	11.41	s
4-OH	8.0	br s	7.9	br s
8-CH_3	2.14	s	2.14	s
9-H_A	2.68	ddd	2.72	ddd
9-H_B	2.84	ddd	2.85	ddd
10-H_A	1.63	dddd	1.63	dddd
10-H_B	1.72	dddd	1.72	dddd
11-H	3.75	ddq	3.75	ddq
11-OH	1.7	br s	1.7	br s
12-CH_3	1.25	d	1.25	d
13-CH_3	2.55	s	2.45	s
14-CH_3	2.45	s	3.93	s

[a] TMS (0 ppm) was used as an internal standard.

All the data described above indicate that the correct structure of resorthiomycin is *S*-methyl 2,4-dihydroxy-3,6-dimethyl-5-(3-hydroxybutyl)-thiobenzoate, as shown in Fig. 1.

Acknowledgments

The authors wish to express sincere thanks to Prof. HARUO SETO of our Institute, The University of Tokyo, for his suggestion and critical reading of this manuscript.

Reference

1) TAHARA, M.; T. OKABE, K. FURIHATA, N. TANAKA, H. YAMAGUCHI, T. NISHIMURA & H. SUZUKI: Resorthiomycin, a novel antitumor antibiotic. II. Physico-chemical properties and structure elucidation. J. Antibiotics 43: 135~137, 1990