

Notes

7-DEMETHYLNAPHTERPIN, A NEW
FREE RADICAL SCAVENGER
FROM *Streptomyces prunicolor*KAZUO SHIN-YA, AKIRA SHIMAZU,
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In the course of our screening for free radical scavengers, we isolated naphterpin (**I**) from *Streptomyces aeriovivifer*¹). It was one of the useful examples to investigate the biosynthesis of terpenoids of actinomycetes origin²), and it consisted of

Table 1. Physico-chemical properties of 7-demethylnaphterpin.

Appearance	Yellow powder
MP (dec)	217~218°C
$[\alpha]_D^{21}$ (c 0.15, CHCl ₃)	-586°
Molecular formula	C ₂₀ H ₂₀ O ₅
HRFAB-MS (<i>m/z</i>)	Calcd: 341.1389 Found: 341.1396 (M+H) ⁺
UV λ_{max}^{MeOH} nm (ϵ)	266 (18,800), 306 (12,400), 410 (4,200)
$\lambda_{max}^{MeOH+NaOH}$ nm (ϵ)	229 (25,200), 292 (20,700), 328 (8,600), 505 (4,200)
IR (KBr) cm ⁻¹	3400, 1620, 1610, 1580, 1280, 1220

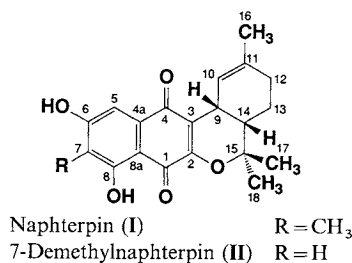
two separated substructures, the naphthoquinone and terpenoid moieties. Further screening has resulted in the isolation of 7-demethylnaphterpin (**II**) from another strain, *Streptomyces prunicolor*, which produced potent free radical scavengers designated benthocyanins³).

A crude ethyl acetate extract of mycelial extract was purified *via* chromatography on a silica gel column using chloroform-methanol (50:1). Further purification on a Sephadex LH-20 column using chloroform-methanol (1:1) gave a pure sample of **II**.

The physico-chemical properties of **II** are shown in Table 1. The molecular formula of **II** was determined as C₂₀H₂₀O₅ by HRFAB-MS ((M+H)⁺, *m/z*, calcd: 341.1389, found: 341.1396). The UV and IR absorptions indicated the presence of a naphthoquinone chromophore as recognized in **I**.

As summarized in Table 2, the ¹³C and ¹H NMR spectral data of **II** are very similar to those of **I**. In

Fig. 1. Structures of 7-demethylnaphterpin and naphterpin.

Table 2. ¹³C and ¹H NMR chemical shifts of 7-demethylnaphterpin.

No.	7-Demethylnaphterpin		Naphterpin		No.	7-Demethylnaphterpin		Naphterpin	
	¹³ C	¹ H	¹³ C	¹ H		¹³ C	¹ H	¹³ C	¹ H
1	183.1		183.1		11	136.1		136.1	
2	153.0		153.5		12	29.7	1.95	29.6	1.95
3	123.8		123.3		13	20.4	1.28, 1.95	20.4	1.25, 1.95
4	183.6		184.8		14	39.7	1.76	39.7	1.75
4a	135.0		131.4		15	80.6		80.8	
5	108.3	7.09	108.4	7.31	16	23.5	1.66	23.5	1.64
6	162.9		161.5		17	25.7	1.55	25.6	1.51
7	107.2	6.53	117.2		18	25.0	1.33	25.1	1.34
8	164.3		162.6		6-OH		6.37		8.25
8a	108.9		107.9		8-OH		11.92		12.20
9	31.1	3.48	31.1	3.47	7-CH ₃			7.8	2.15
10	120.0	6.04	120.0	6.01					

ppm from internal TMS in CDCl₃.

the ^1H NMR spectrum of **II**, however, the methyl singlet signal assignable to 7- CH_3 (2.15 ppm) in **I** was replaced by an olefinic singlet proton 7-H (6.53 ppm) *meta*-coupled to 5-H (7.09 ppm, $J=2$ Hz). The ^{13}C NMR spectrum of **II** also supported the disappearance of 7- CH_3 (7.8 ppm) observed in **I**. Thus, the quaternary carbon C-7 (117.2 ppm) in **I** was replaced by a protonated carbon (107.2 ppm) in **II**. These data suggested that the structure of **II** was a demethylated derivative of **I** at the C-7 position.

The absolute stereochemistry of **II** was deduced to be the same as that of **I** based on the similar optical rotation values ($[\alpha]_D^{21} -586^\circ$ (c 0.15, CHCl_3); *cf.* **I**, $[\alpha]_D^{23} -648^\circ$ (c 0.1, CHCl_3)), and is as shown in Fig. 1.

The activity of **II** to inhibit lipid peroxidation in rat liver microsomes was almost the same as that of **I**; IC_{50} values of **II** and **I** were 9.0 $\mu\text{g}/\text{ml}$ and 5.3 $\mu\text{g}/\text{ml}$, respectively, while that of vitamin E was 9.3 $\mu\text{g}/\text{ml}$. Thus, the methyl residue at C-7 does not affect the radical scavenging activity of the naphterpins.

Although **II** was isolated from *Streptomyces prunicolor*, **I** could not be detected as a metabolite of this microorganism so far tested, while a trace of **II** was produced by *Streptomyces aeriouvifer* (about

1% of the amount of **I**). In addition, **II** was produced in a high yield by some mutants of *Streptomyces aeriouvifer* that produced a trace of naphterpin (unpublished data). These phenomena indicated that **II** is reasonably assumed to be a precursor of **I**.

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