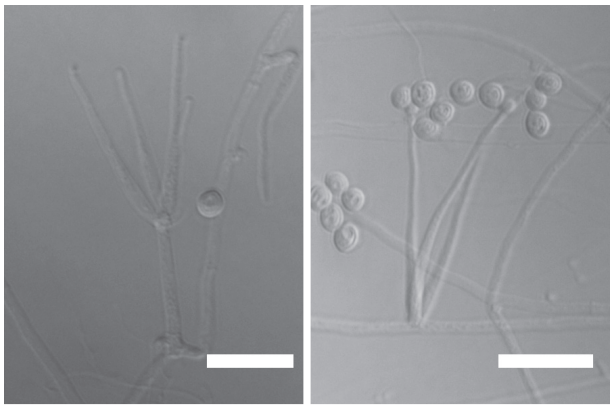
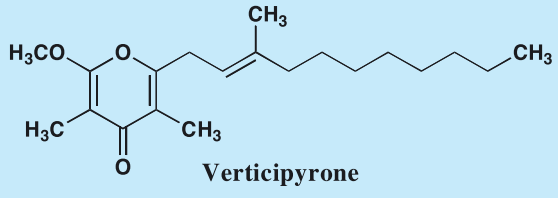
Verticipyrone

1. Discovery, producing organism and structure[1-4)]

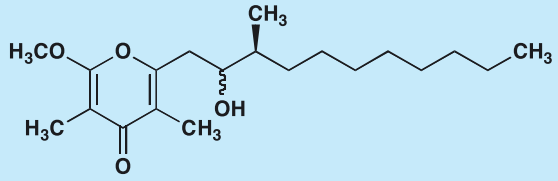
A new NADH-fumarate reductase inhibitor, verticipyrone, was isolated from the culture broth of *Metapochonia rubescens* FKI-1083. Verticipyrone inhibited both Ascaris and bovine heart complex I, and its synthetic analogue, 9-hydro-8-hydroxyverticipyrone, showed good selectivity against *Ascaris* complex I.



Verticillium sp. FKI-1083
(*Metapochonia rubescens* FKI-1083)
Bars: 10 μm)



Verticipyrone



9-Hydro-8-hydroxyverticipyrone

2. Physical data

Colorless oil. $C_{20}H_{32}O_3$; mol wt 320.47. Sol. in MeOH, EtOAc, $CHCl_3$. Insol. in H_2O, hexane.

3. Biological activity[1)]

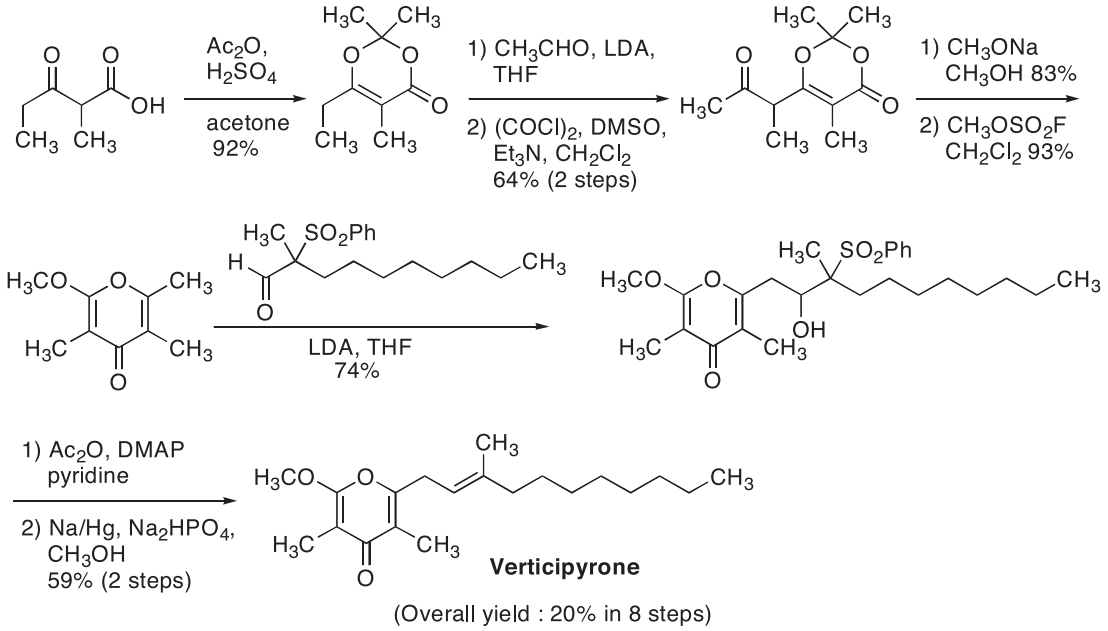
1) Inhibitory activity against electron transport enzymes

Origin	Enzyme	Complex	IC_{50} [nM]	
			Verticipyrone	9-Hydro-8-hydroxy-verticipyrone
Ascaris suum	NADH-fumarate reductase	I+II	0.88	1.5
	NADH-rhodoquinone oxidoreductase	I	49	2.0
	Rhodoquinol-fumarate oxidoreductase	II	>100,000	>100,000
Bovine heart	NADH oxidase	I+III+IV	1.3	20
	NADH-ubiquinone oxidoreductase	I	46	200
	Succinate-ubiquinone oxidoreductase	II	>100,000	>100,000
	Ubiquinol-cytochrome c oxidoreductase	III	26,000	80,000

2) Minimum growth inhibitory concentrations of verticipyrone against *Caenorhabditis elegans* and *Artemia salina* were 20 μg/ml and 2.0 μg/ml, respectively. Verticipyrone exhibited moderate antimicrobial activity against Gram-positive bacteria.

4. Total synthesis[2)]

Below is scheme of the first total synthesis of verticipyrone achieved by Ōmura's group (See Appendix-I).



5. References

1. [934] H. Ui *et al*., *J*. *Antibiot*. **59**, 785-790 (2006)
2. [938] H. Shimamura *et al*., *Org*. *Lett*. **9**, 65-67 (2007)
3. [1149] K. Nonaka *et al*. *Mycologia* **105**, 1202-1218 (2013)
4. R. M. Kepler *et al*. *Mycologia* **106**, 811-829 (2014)