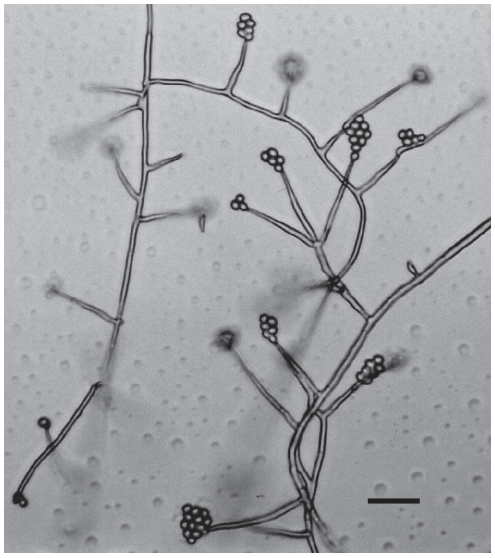
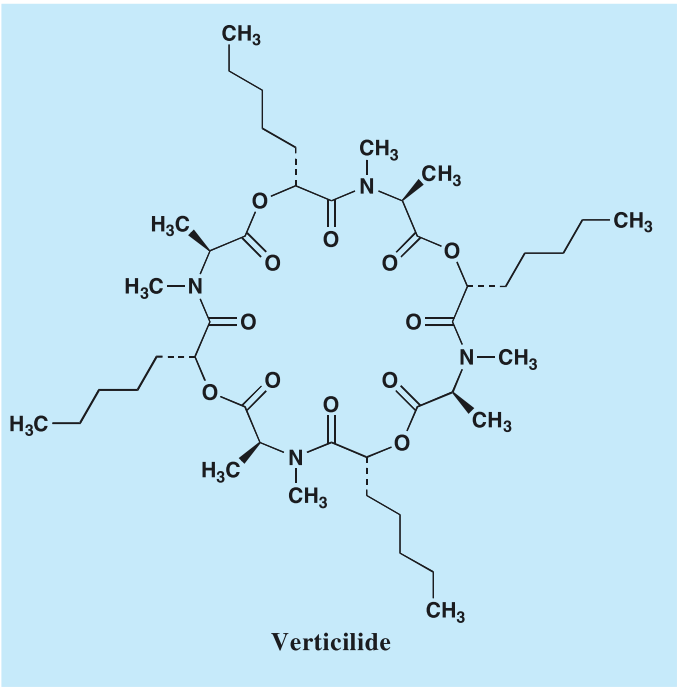
# Verticilide

## 1. Discovery, producing organism and structure[1-3)]

Verticilide was isolated from the culture broth of a fungus, *Acremonium variecolor* FKI-1033, during screening of ryanodine binding inhibitor. It showed selective ryanodine binding inhibition to insect ryanodine receptor[1,3)]. The structure of verticilide was elucidated as a 24-membered ring cyclic depsipeptide, and the absolute configuration of the 2-hydroxyheptanoic acid was revealed synthetically[2)].



*Verticillium* sp. FKI-1033
(*Acremonium variecolor* FKI-1033)
Bar: 10 $\mu$m)



Verticilide

## 2. Physical data

Colorless oil. $C_{44}H_{76}N_4O_{12}$; mol wt 853.09. Sol. in MeOH, EtOH, EtOAc, $CHCl_3$. Insol. in $H_2O$, hexane.

## 3. Biological activity[1,3,4)]

1) Inhibitory activity against ryanodine receptor[1,3)]

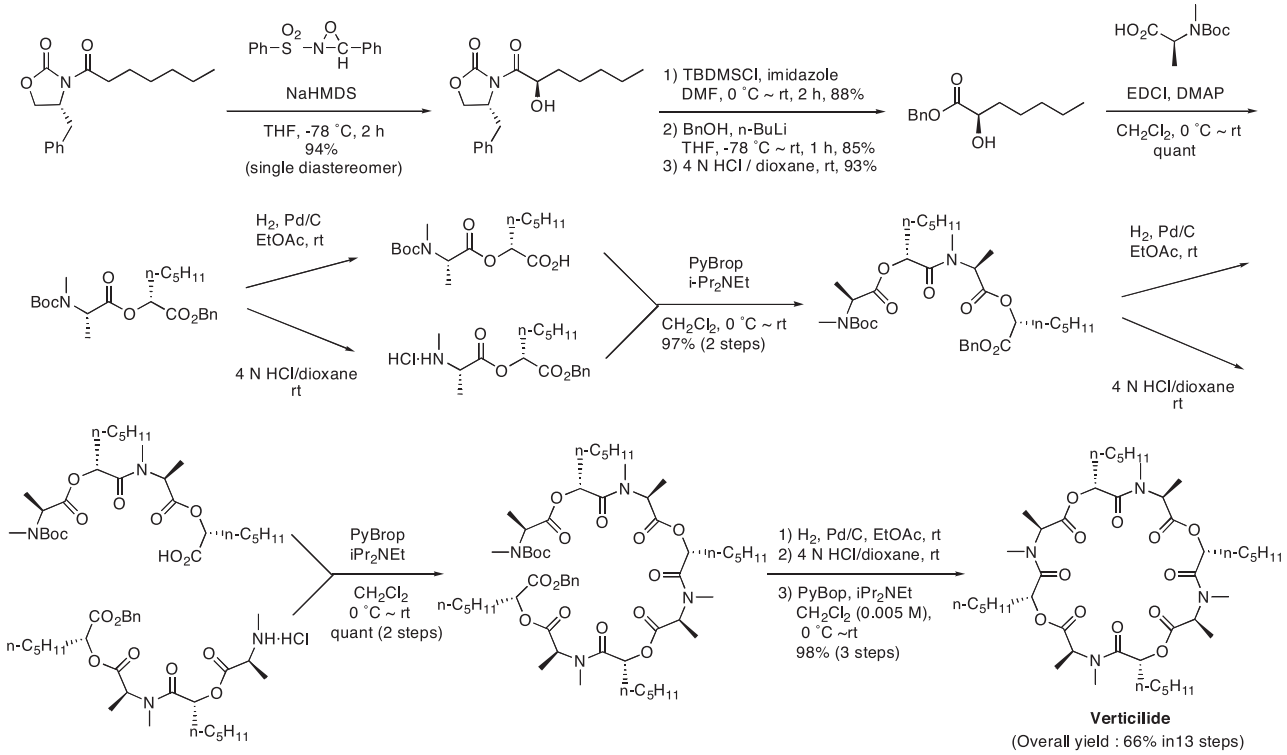
Verticilide showed dose dependent ryanodine binding inhibition against cockroach receptor at the $IC_{50}$ value of 4.2 $\mu$M. The $IC_{50}$ value against mouse leg receptor was 53.9 $\mu$M. The other 24-membered ring cyclic depsipeptides (bassianolide and PF1022A) did not show ryanodine binding inhibition against cockroach receptor at 100 $\mu$M.

2) Verticilide caused mortality in *Caenorhabditis elegans* and *Artemia salina* at 20 $\mu$g/ml. Verticilide showed no antibacterial or antifungal activity.[1)]

3) Verticilide A and its analogs showed selective inhibition toward ACAT2, with $IC_{50}$ 8.5-11-fold more potent than observed against ACAT1.[4)]

## 4. Total synthesis[2)]

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




## 5. References


1. S. Ōmura *et al*., WO 2004/044214 (2004)
2. [926] S. Monma *et al*., *Org*. *Lett*. **8**, 5601-5604 (2006)
3. [1059] K. Shiomi *et al*., *J*. *Antibiot*. **63**, 77-82 (2010)
4. T. Ohshiro *et al*., *J*. *Antibiot*. **65**, 255-262 (2012)