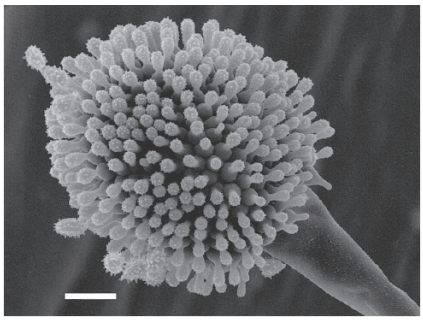
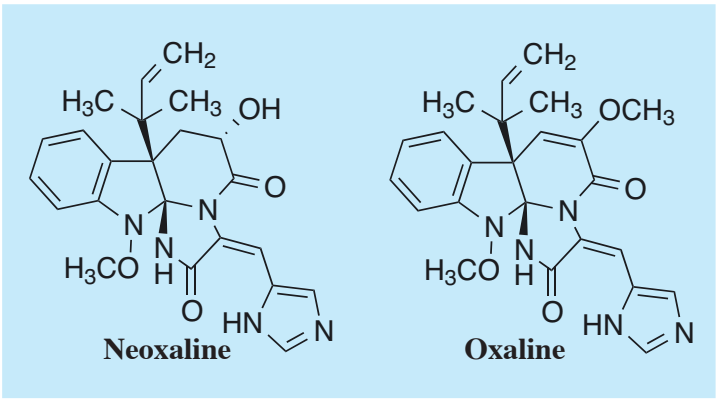
Neoxaline ©

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

Neoxaline and a similar compound, oxaline,[3)] were isolated from the culture broth of *Aspergillus japonicus* Fg-551 while screening for Dragendorff's reagent positive-substances.



Aspergillus japonicus Fg-551
Bar: 5 μm



2. Physical data (Neoxaline)[1)]

Colorless needles. $C_{23}H_{25}N_5O_4$; mol wt 435.19. Sol. in MeOH, $CHCl_3$. Insol. in benzene.

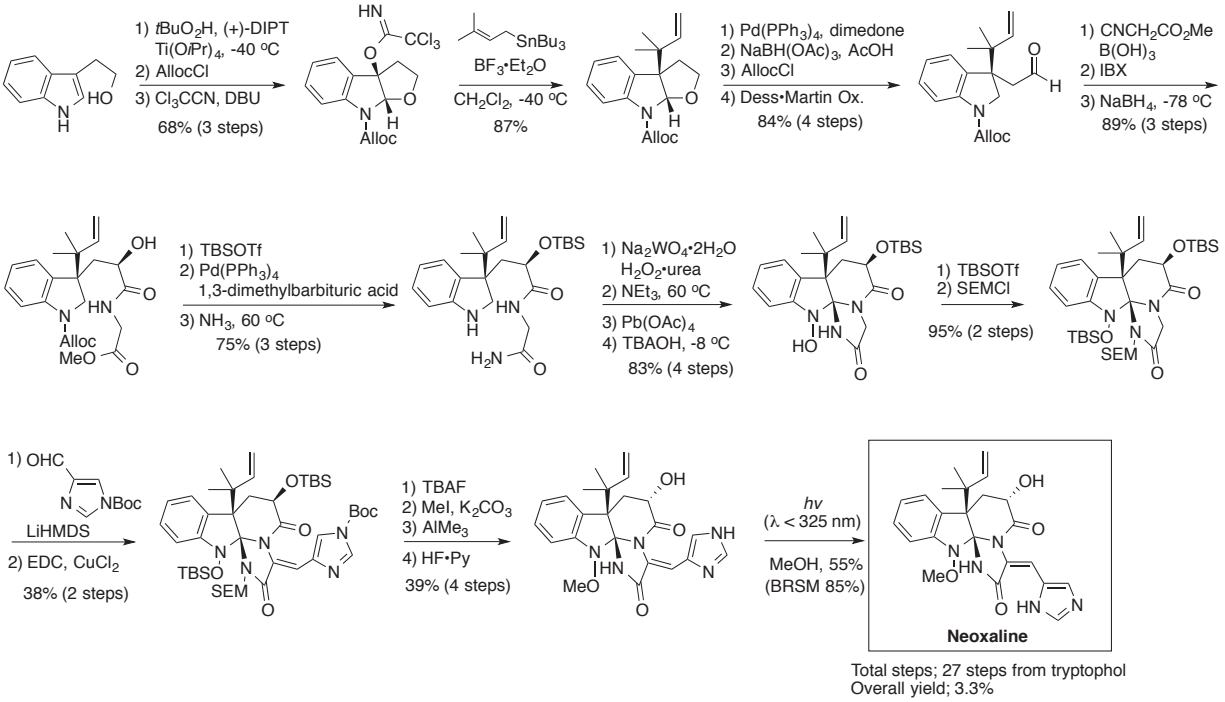
3. Biological activity[1,4)]

Neoxaline did not have antibacterial or antifungal activity at concentrations of 500 μg/ml. The acute toxicity (LD_{50}) of the compound by intraperitoneal administration in mice was greater than 200 mg/kg[1)].

Recently, neoxaline and oxaline were found to inhibit cell proliferation and arrest the cell cycle at the M phase in Jurkat cells. Oxaline bound to tubulin at or near the colchicine binding site, resulted in inhibition of tubulin polymerization[3)].

5. Total synthesis[5,6)]

The total synthesis of neoxaline has been achieved by Ōmura group.[6)] (See Appendix I)



Total steps; 27 steps from tryptophol
Overall yield; 3.3%

6 Reference

1. [163] A. Hirano *et al*., *J*. *Antibiot*. **32**, 781-785 (1979)
2. [194] Y. Konda *et al*., *Chem*. *Pharm*. *Bull*. **28**, 2987-2993 (1980)
3. D. W. Nagel *et al*., *J*. *Chem*. *Soc*., *Chem*. *Commun*. 1021-1022 (1974)
4. [879] Y. Koizumi *et al*., *Biochim*. *Biohys*. *Acta* 1693, 47-55 (2004).
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6. [1156] T. Ideguchi *et al*., *J*. *Am*. *Chem*. *Soc*. **135**, 12568-12571 (2013)