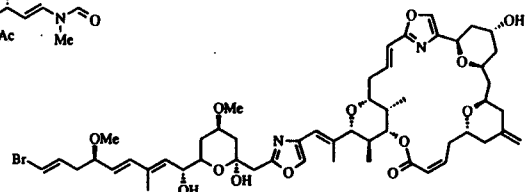
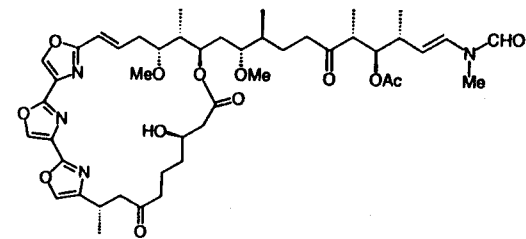


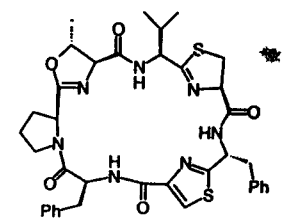
Ulapualide A



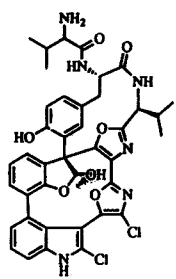
Phorboxazole A



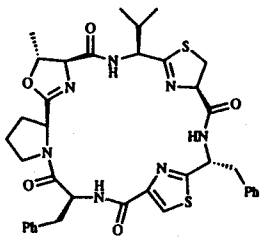
Ulapualide A



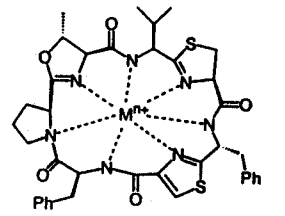
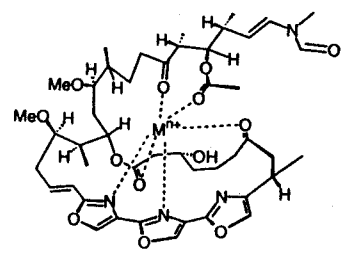
Lissoclinamide 4



Diazonamide A

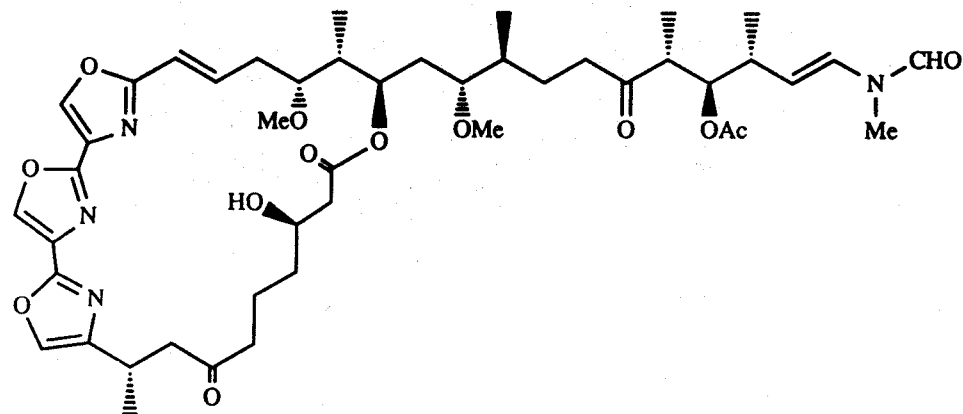


Lissoclinamide 4



Metal Ions in Biological Systems

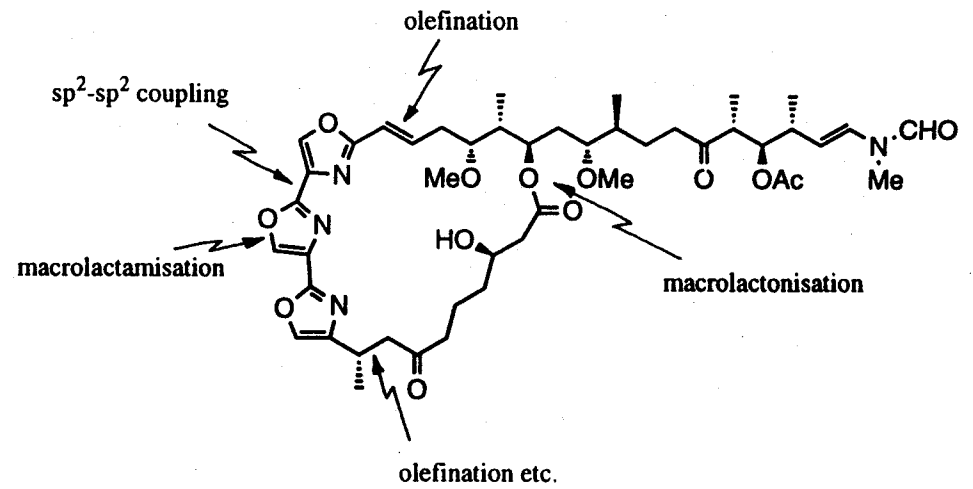
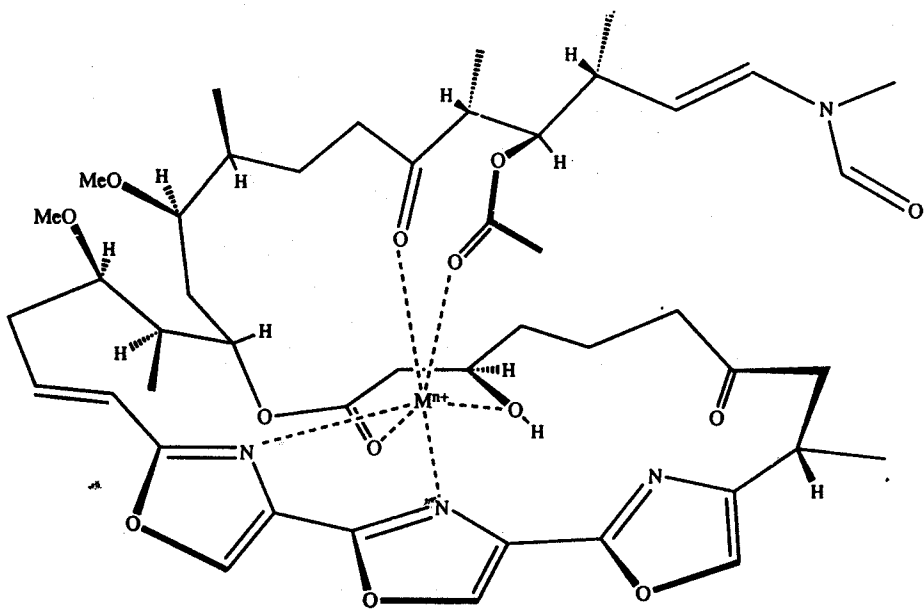
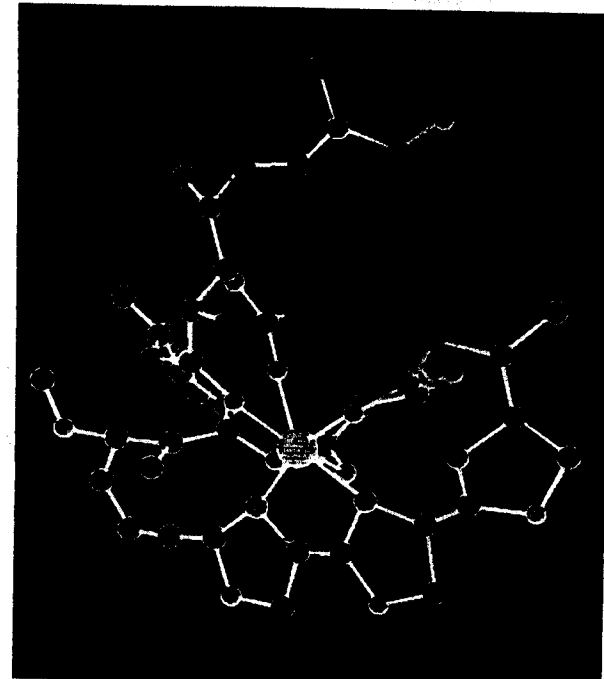
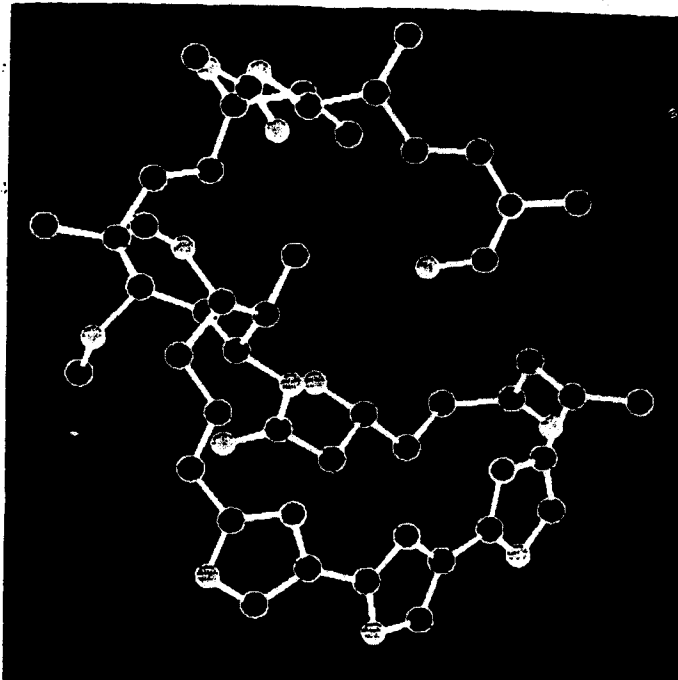
Na, K	Mg, Ca	Zn	Fe, Cu, Mo	Co
Charge-carriers	Structure formers and triggers	Lewis acid	Redox Catalysts	Isomerases and Synthetases
Mobile	Semi-mobile	Static	Static	Static
Oxygen-anion binding		Nitrogen / sulphur ligands		Nitrogen ligands

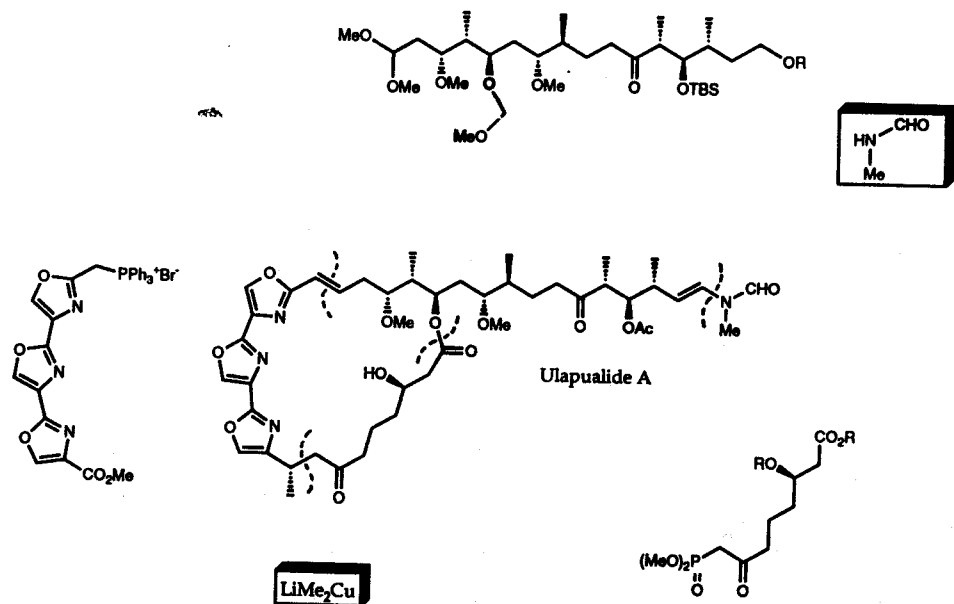


"Ulapualide A"

cf Kabiramide ; ex Hexabranchnus sanguineus

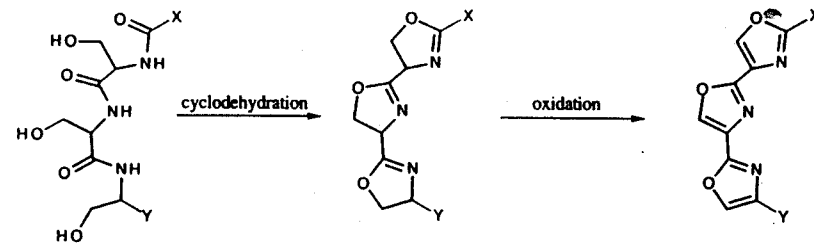
Halichondramide ; ex Halichondria sp.



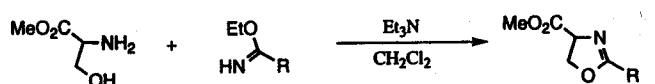
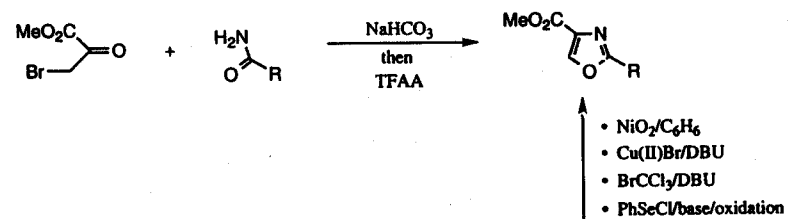
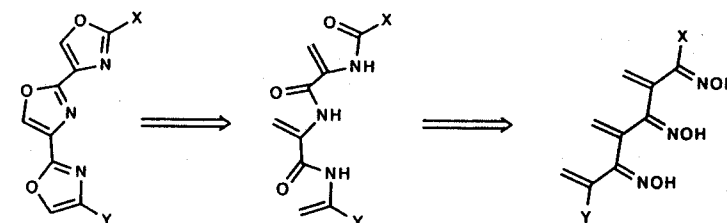


Biosynthesis of the tris-Oxazole Unit ?

• Cyclisation of a tris-serine moiety



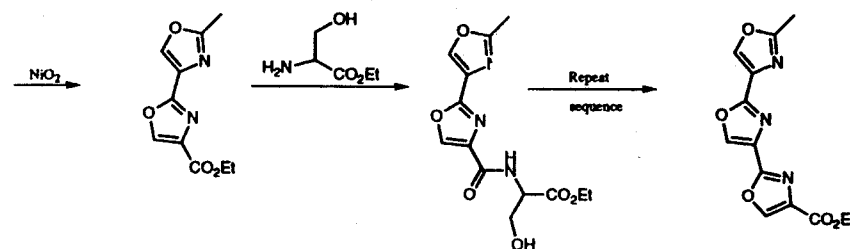
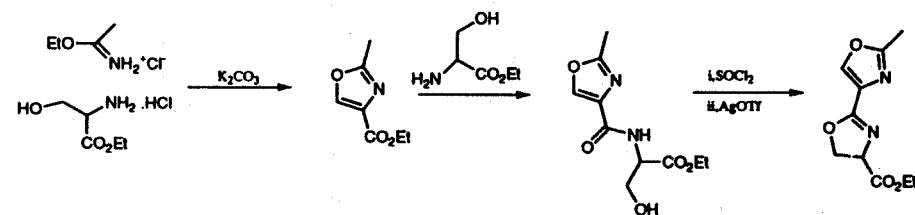
• Rearrangement of a tris-oxime derived from a β -ketide



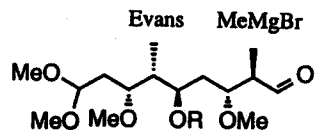
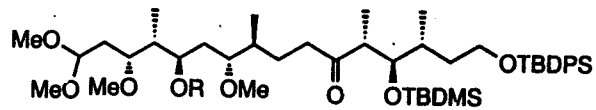
- $\text{SOCl}_2/\text{AgOTf}$
- DAST
- Burgess
- POCl_3
- $\text{MeSO}_2\text{Cl}/\text{Et}_3\text{N}$

cf • aziridine formation
• dehydration

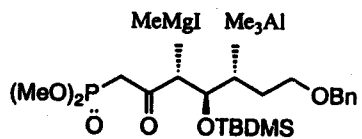
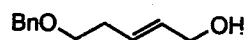
Burgess = $\text{MeO}_2\text{C}-\text{N}^+-\text{SO}_2\text{NEt}_3$



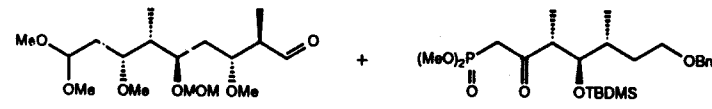
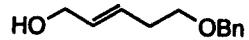
Tris-oxazole portion



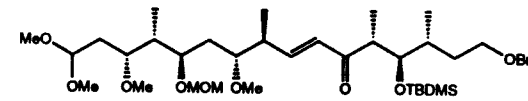
Brown Evans anti-aldol Sharpless



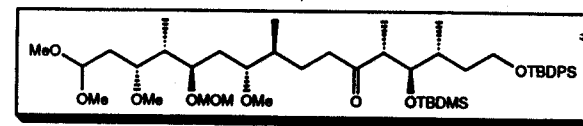
(Sharpless) Sharpless



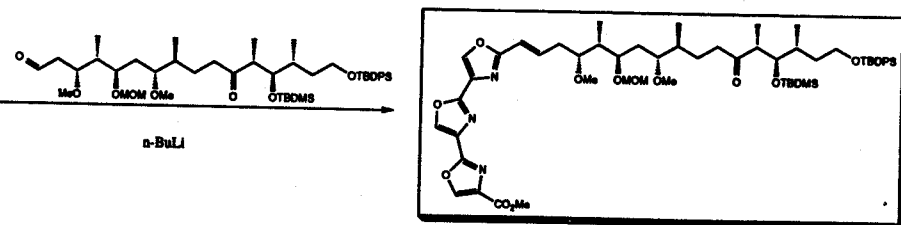
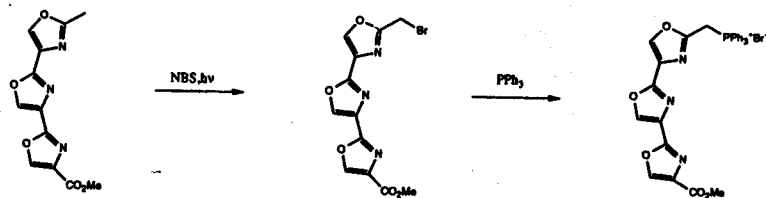
Ba(OH)_2 ; wet THF



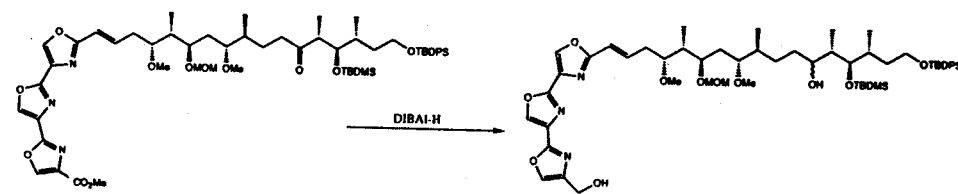
$\text{LH}_2/\text{Pd-C}$
 H.TBDPS-Cl



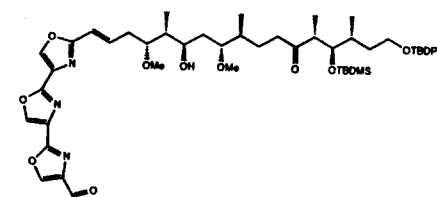
Ulapualide Side Chain

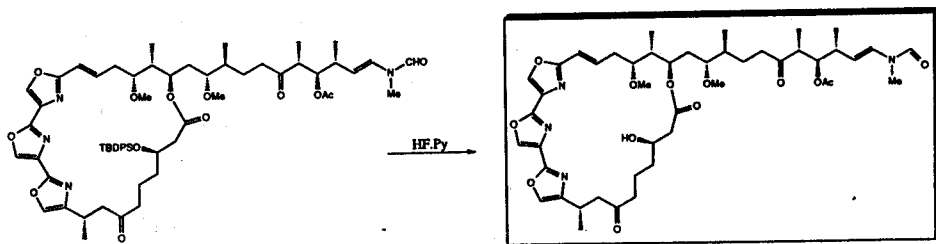
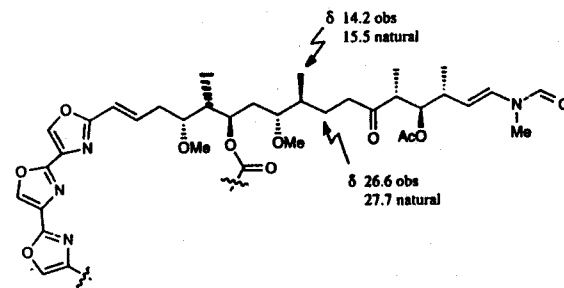
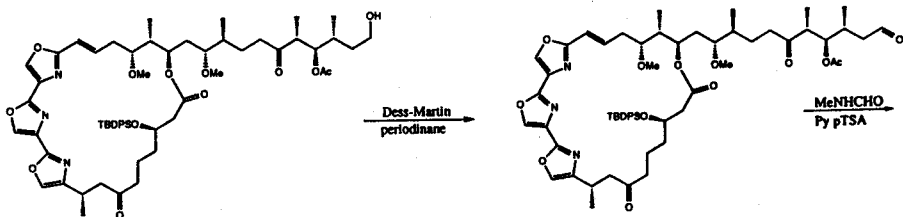
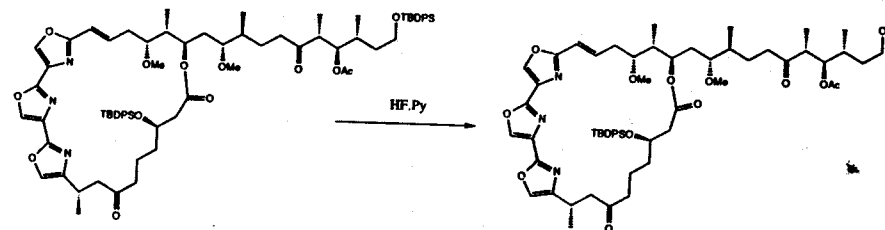
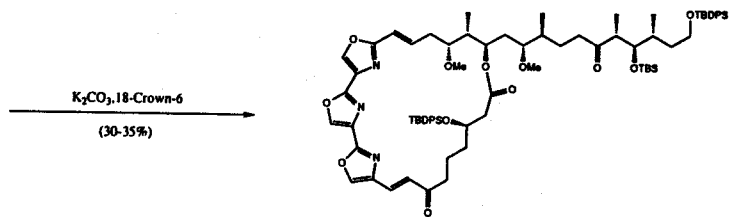
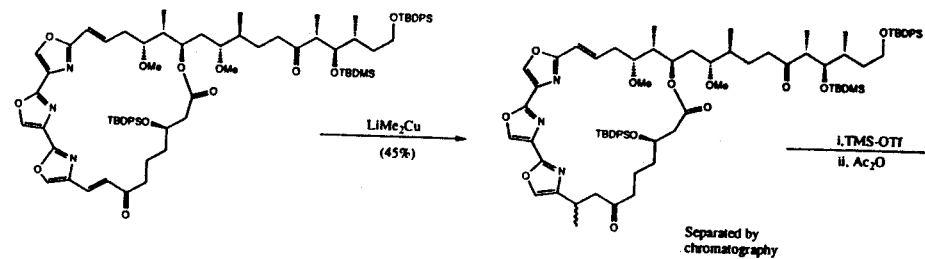
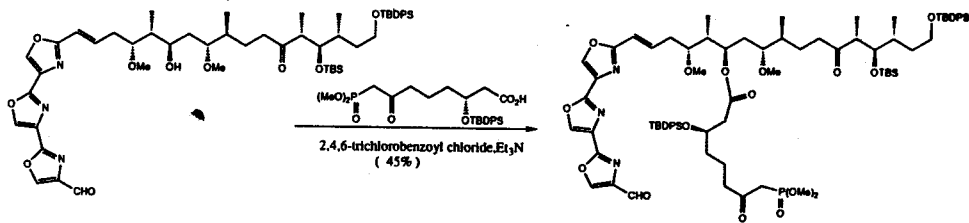


73%; < 5% Z- isomer

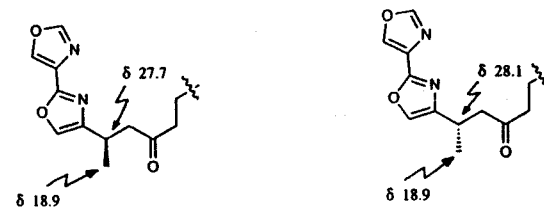


1,2-Dess-Martin oxidation
ii. Me_3BBr

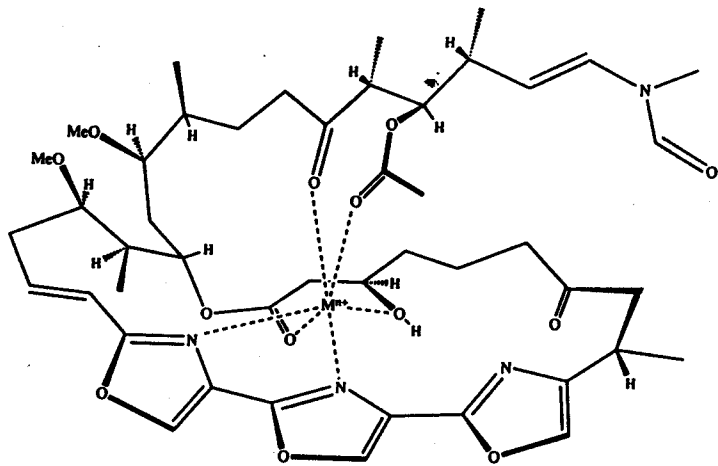




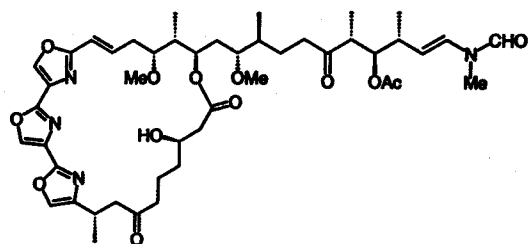
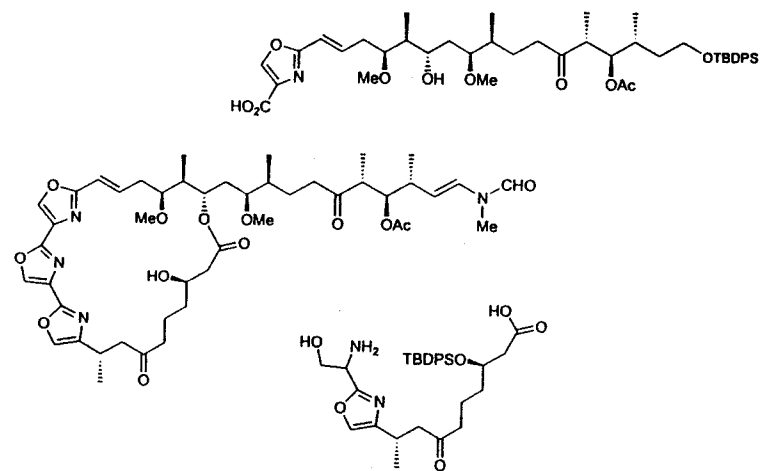
Utapualide A



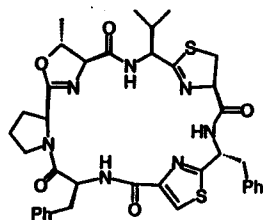
[Natural δ 18.9 and δ 27.6 p.p.m.]



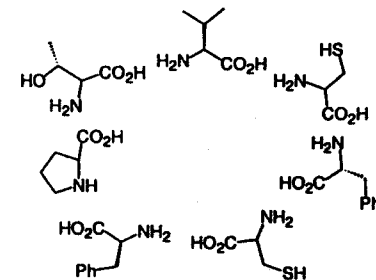
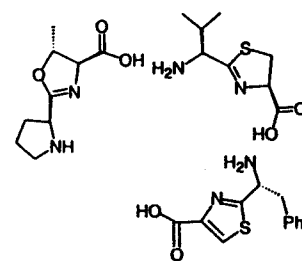
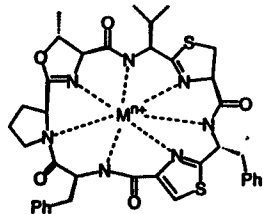
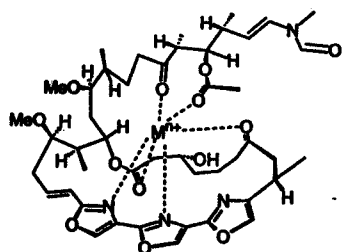
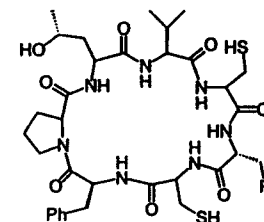
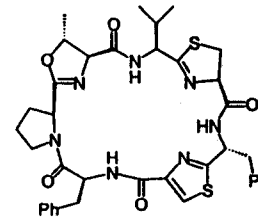
Cu 3×10^3
 Ag 6×10^4 [cf Siderophore 1×10^3]
 Fe 5×10^4 [cf 18-Crown-6 (K_2^+) 3×10^5]



Utapualide A

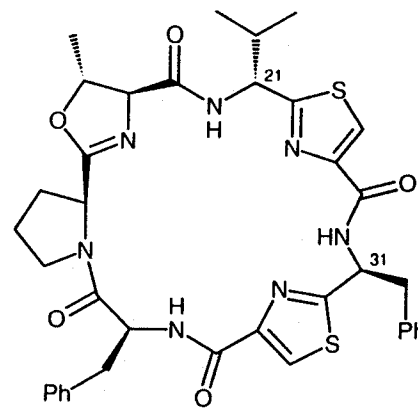


Lissoclinamide 4

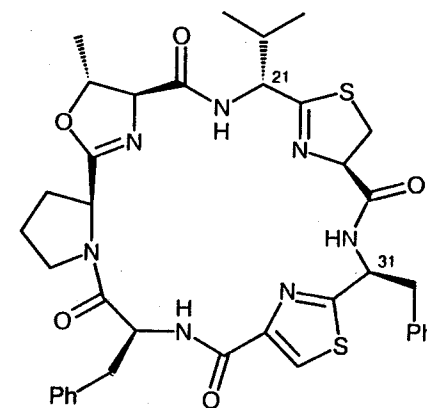




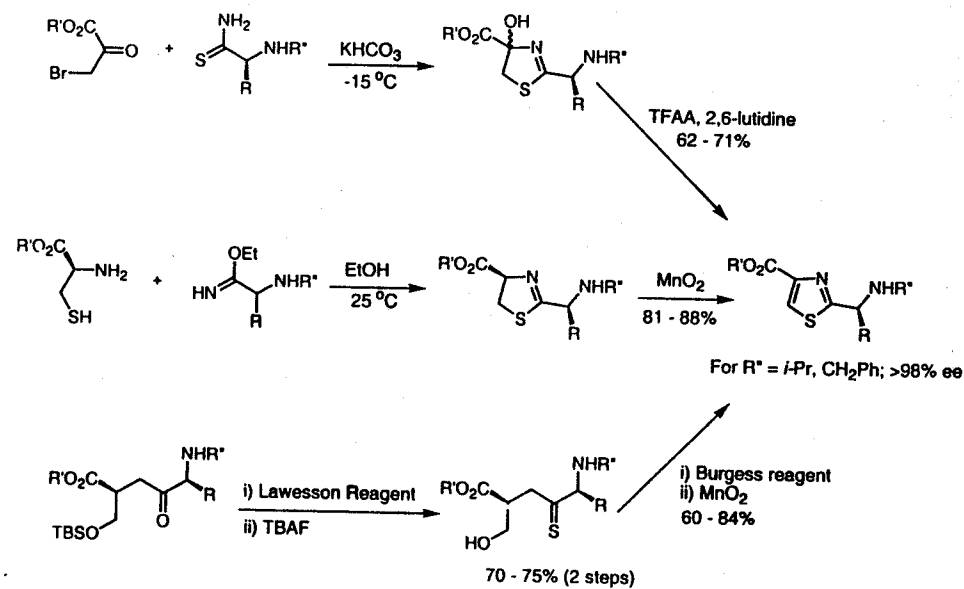
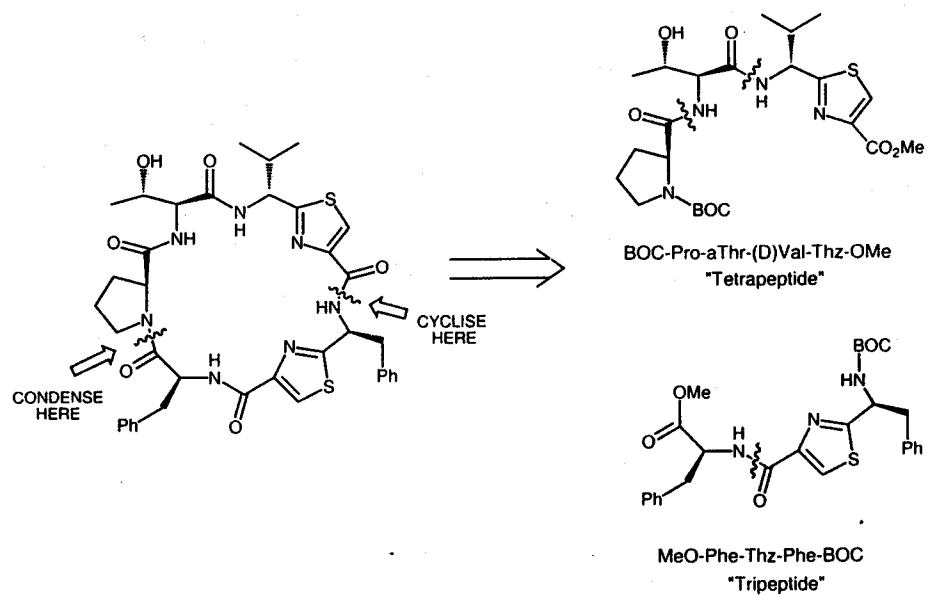
Lissoclinamides 5 and 4 - Structures Predicted from NMR and Partial Sequencing

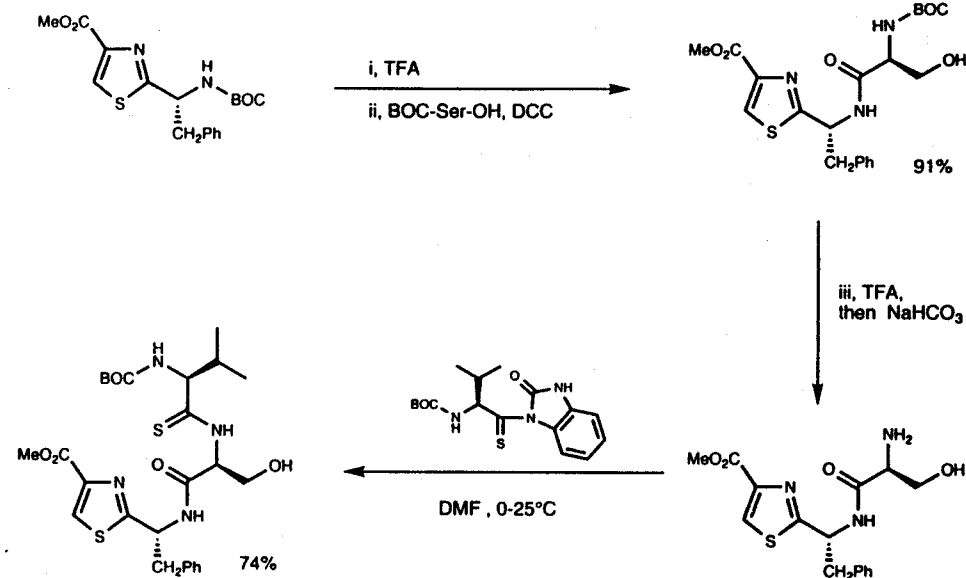
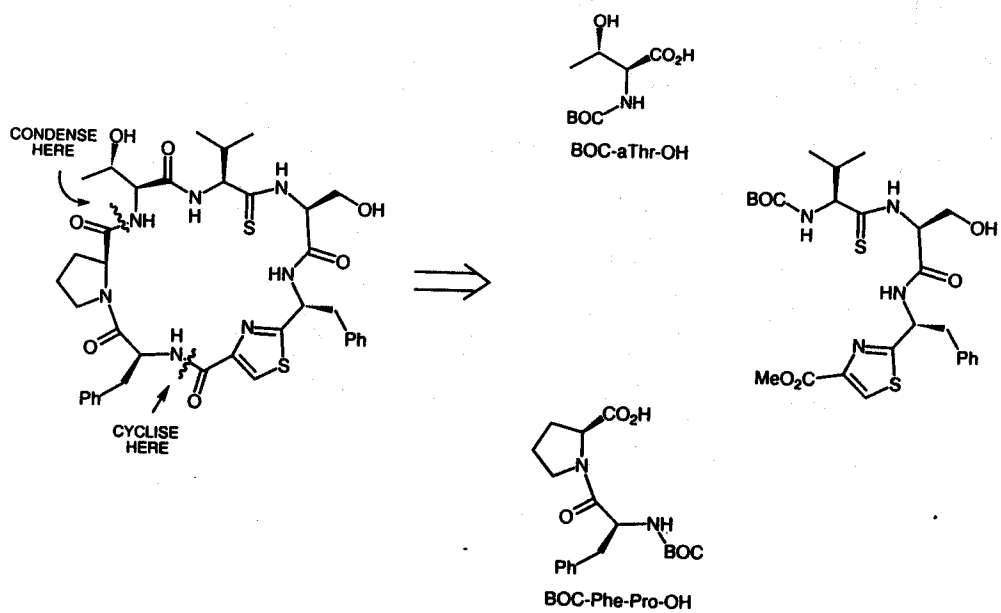
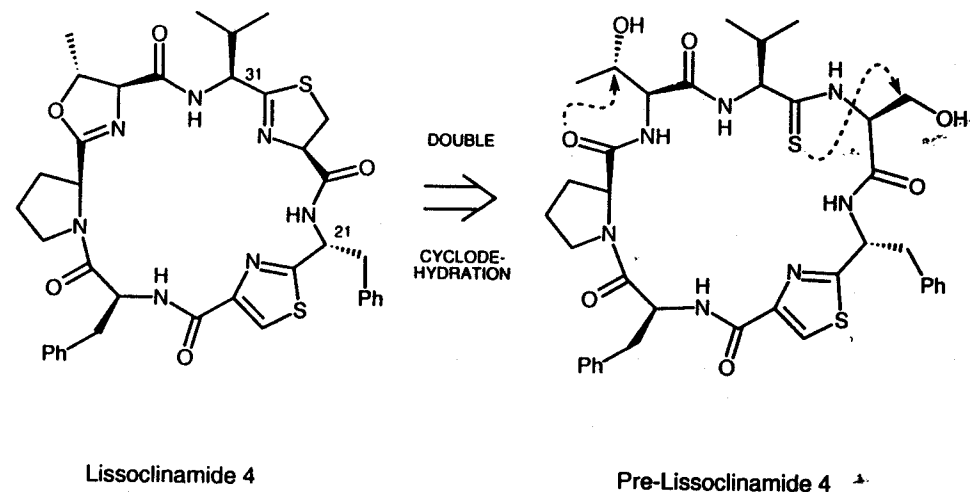
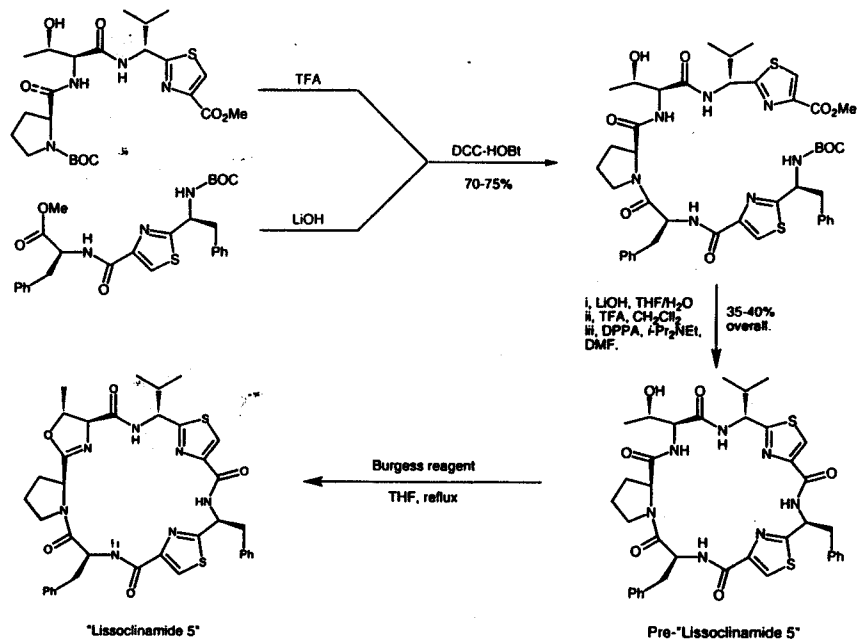


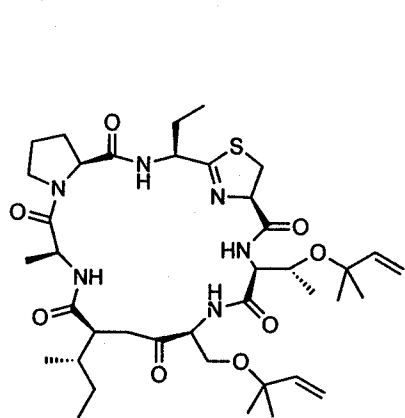
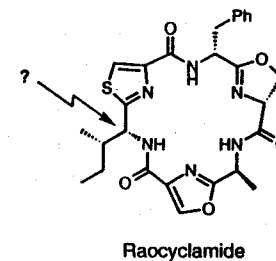
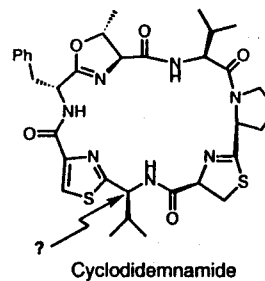
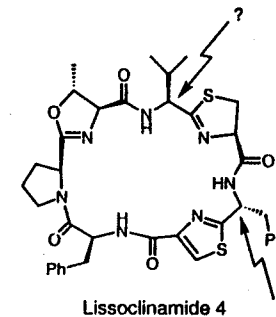
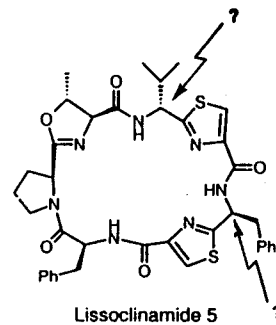
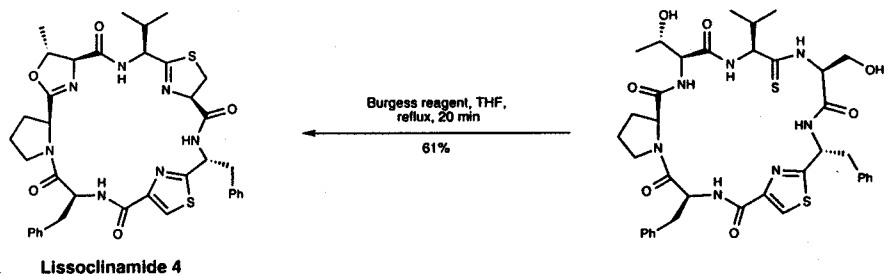
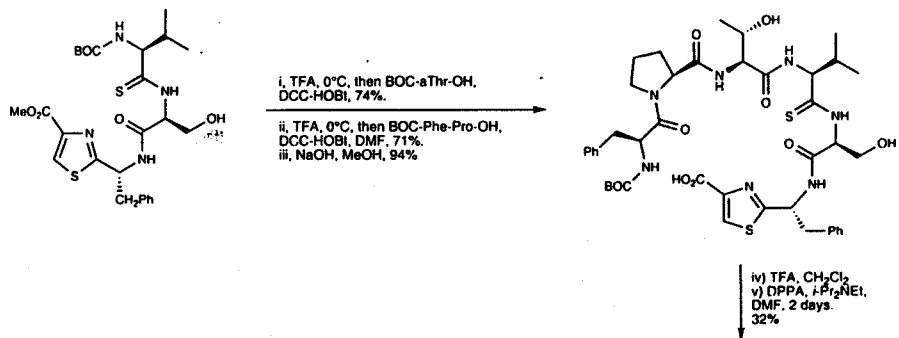
Lissoclinamide 5



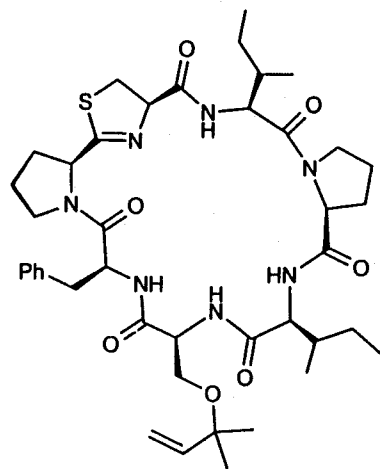
Lissoclinamide 4



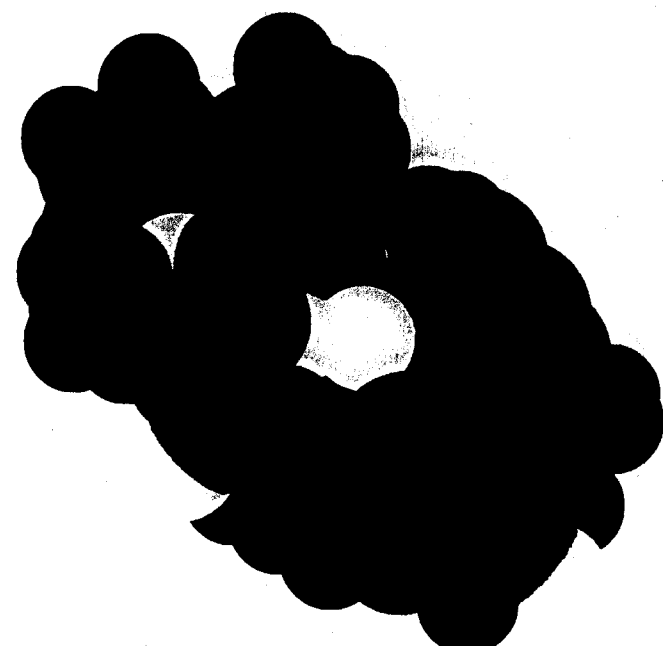




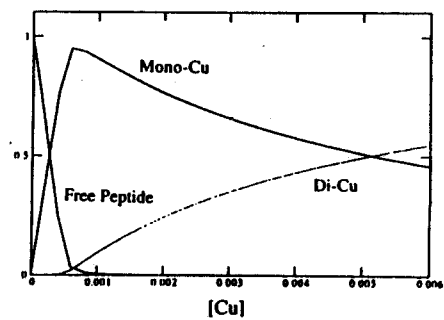
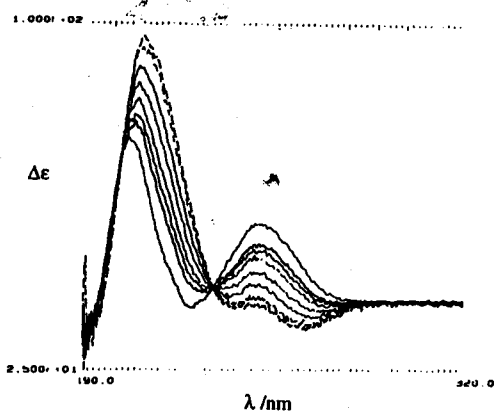
Trunkamide
 ex. ascidian *Lissoclinium* sp.
 cytotoxic and anti-bacterial activity



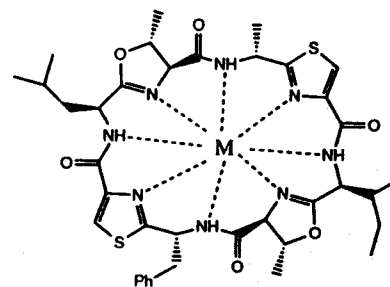
Mollamide
 ex. ascidian *Didemnum molle*.
 cytotoxic activity against a range of cell lines



Circular Dichroism Studies of Patellamide B-Copper Interactions

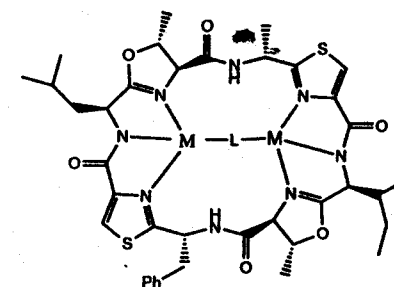


Metal-Cyclopeptide Interactions?



M=Cu, Zn

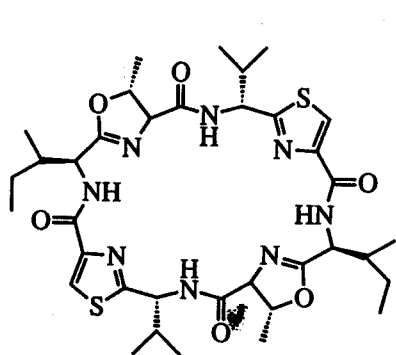
Cu : $K_1 = 3 \times 10^5$
 Zn : $K_1 = 3 \times 10^4$



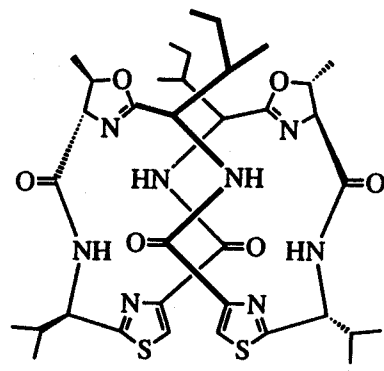
Cu : $K_2 = 2 \times 10^2$
 Zn : $K_2 = 2 \times 10^1$

cf. 18-Crown-6 (K^+): $K_1 = 1.3 \times 10^6$

Patellamide Conformations

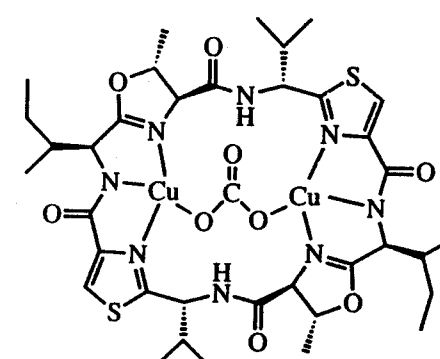
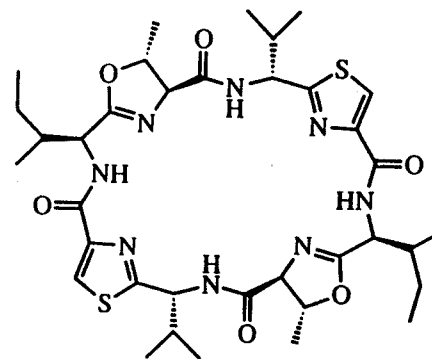


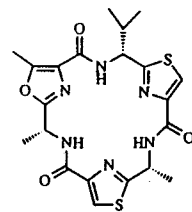
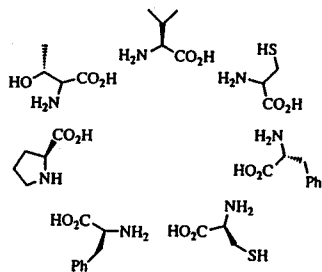
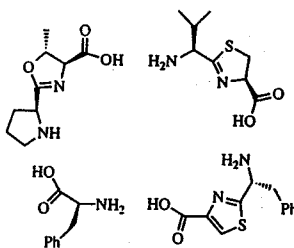
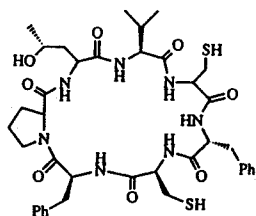
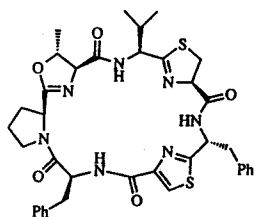
Square Geometry



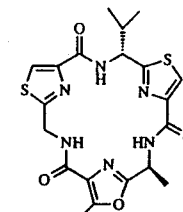
Twisted Figure of 8 Geometry

Asciacyclamide and Copper Complex



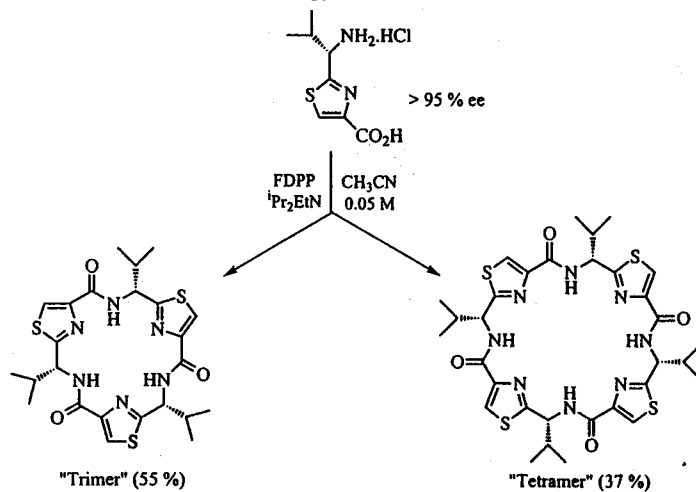


Dendroamide A
ex. *Stigonema dendroideum*

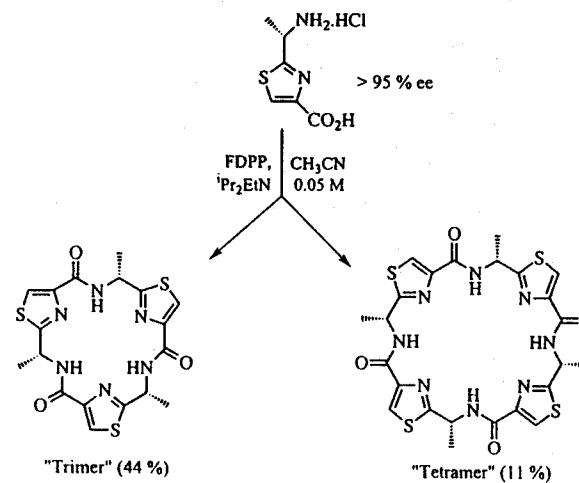


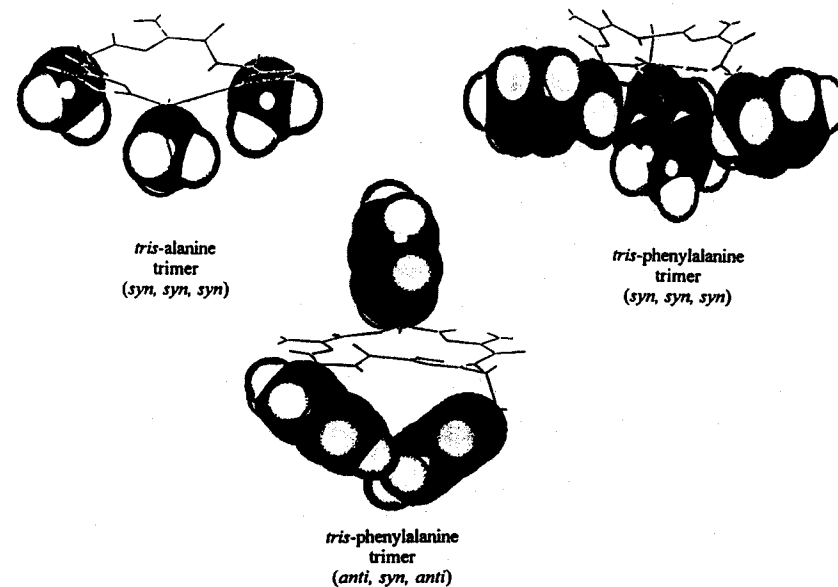
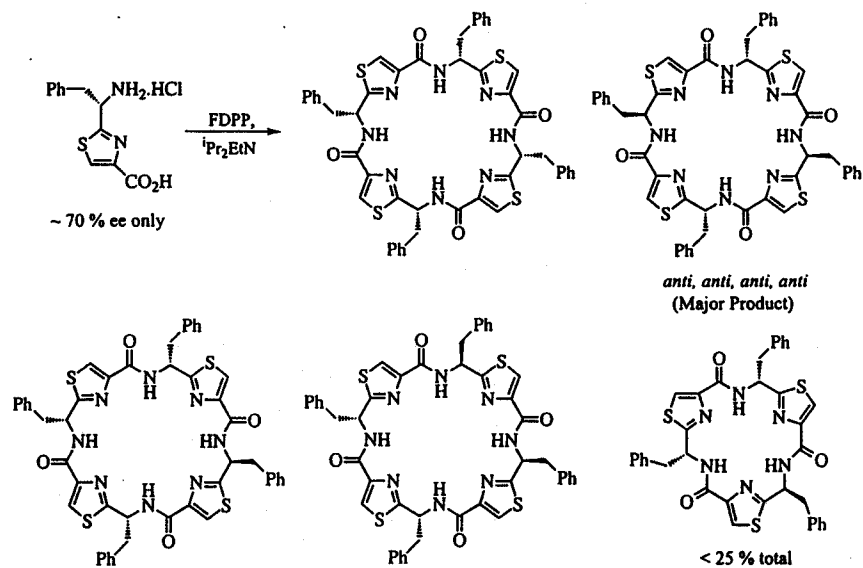
Nostacyclamide
ex. cyanobacterium *Nostoc* sp.

Thiazole Cyclooligomerisation (*iso*-Propyl; valine)

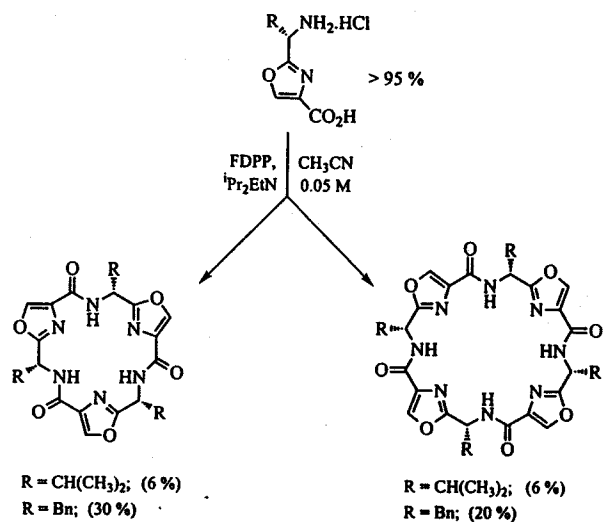


Thiazole Cyclooligomerisation (methyl; alanine)

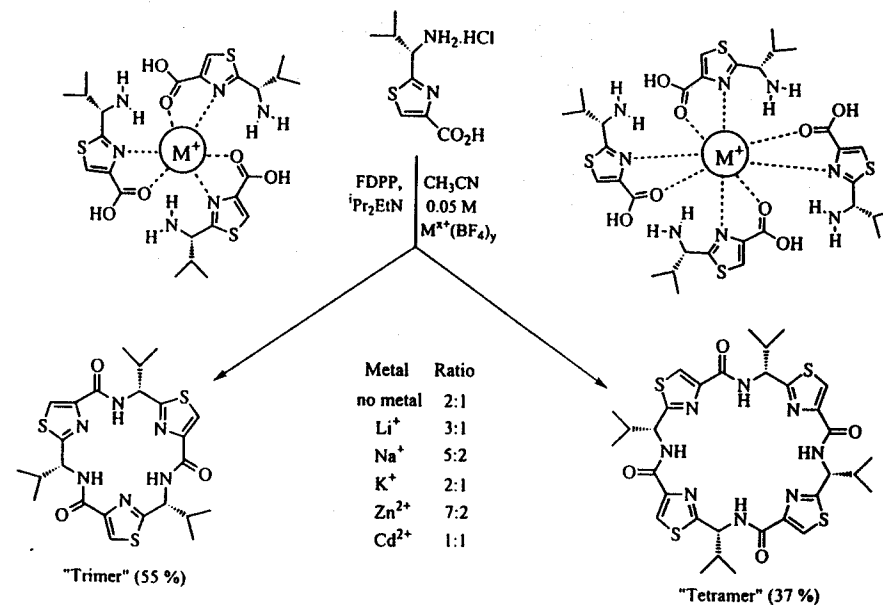


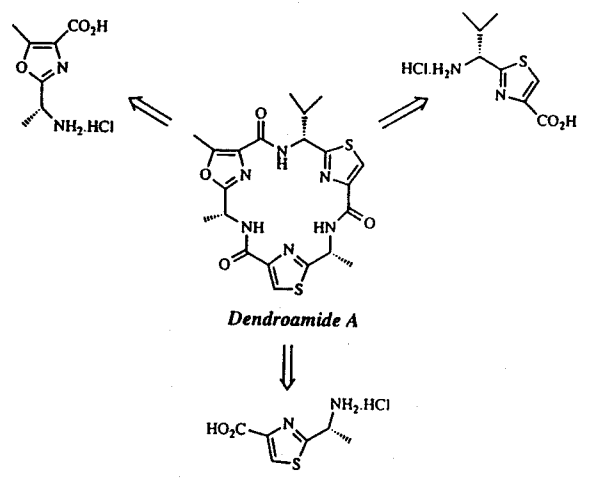


Oxazole Cyclooligomerisation

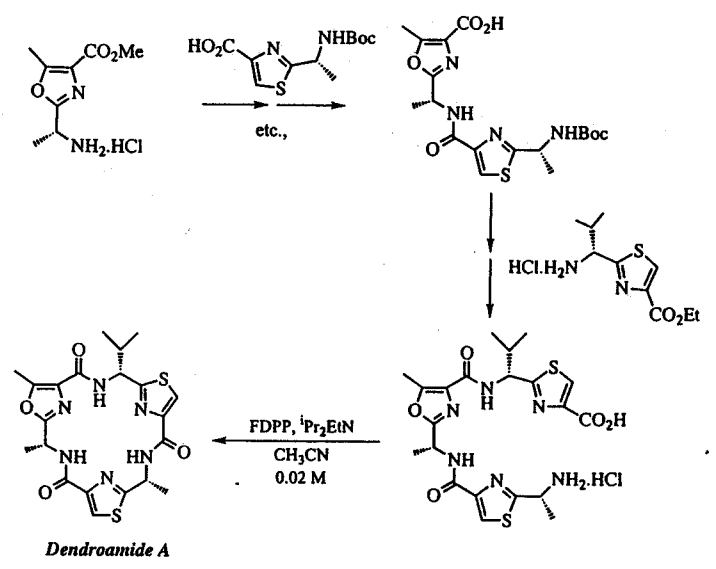


Metal Templated Cyclisations





Dendroamide A : Linear Synthesis



Dendroamide A : "Self-assembly"

