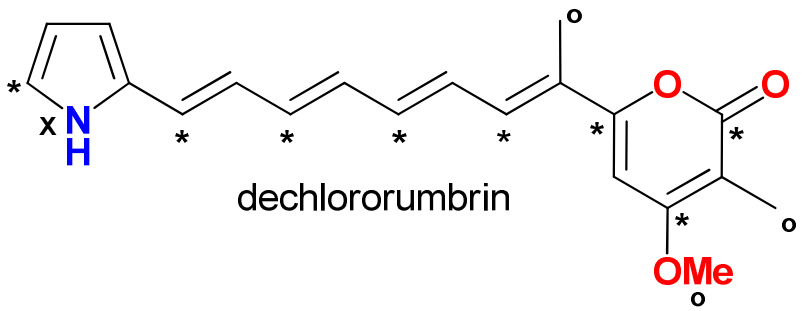
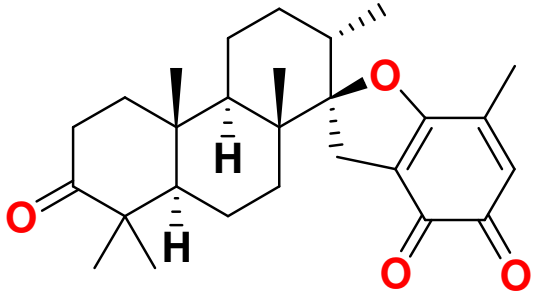
Natural Products Isolation and Drug Discovery





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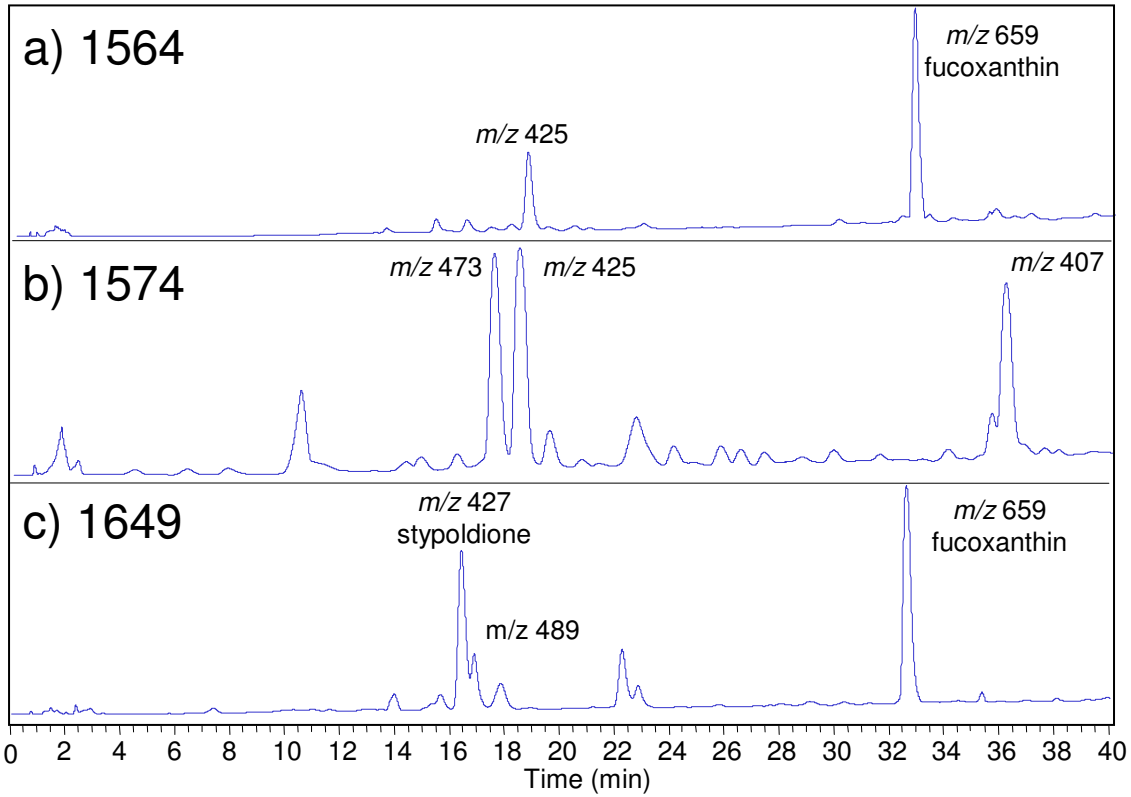
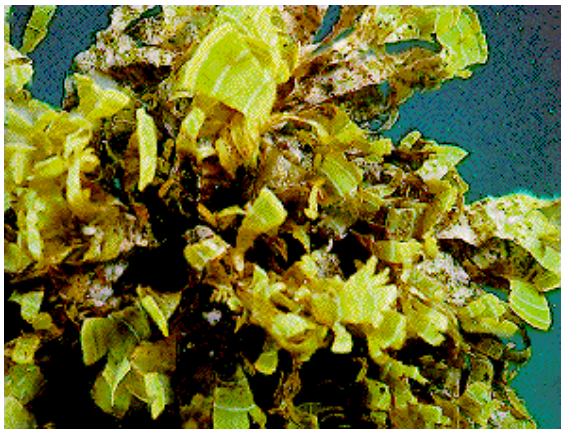
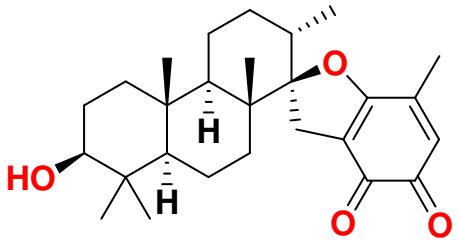
Stypopodium metabolites

- Genus of tropical red algae
  - produce characteristic meroterpenoid metabolites
  - Three strains analysed by LC-MS



LCMS analysis of *Stypopodium* isolates

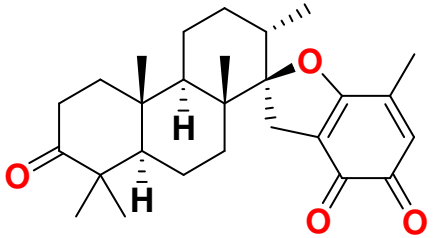




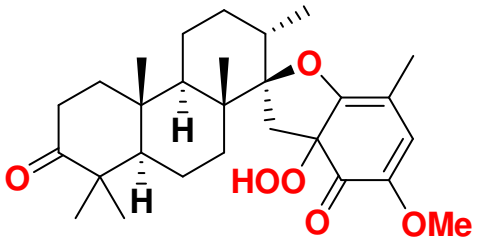
stypoldione

New Meroterpenoids

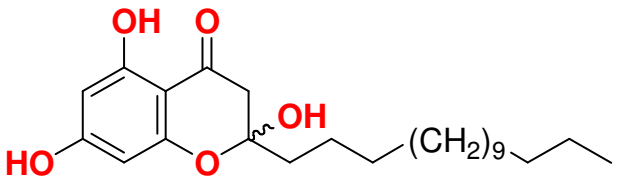
- Four new metabolites isolated
  - HDAC and MCL-1 inhibitory activity
  - Derived from more active precursors?



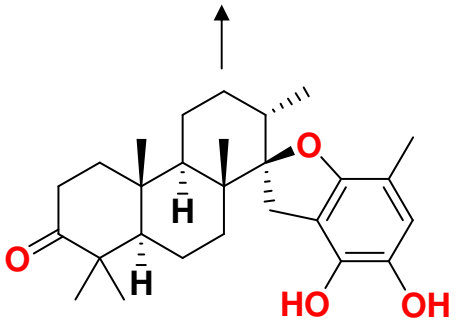
stypoltrione



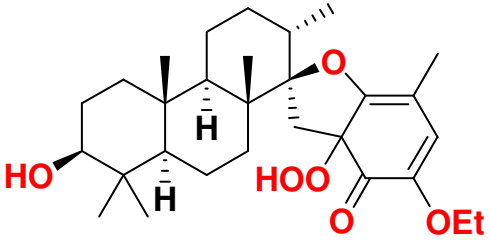
14-ketostypohydroperoxide



chromanone



stypodiolone

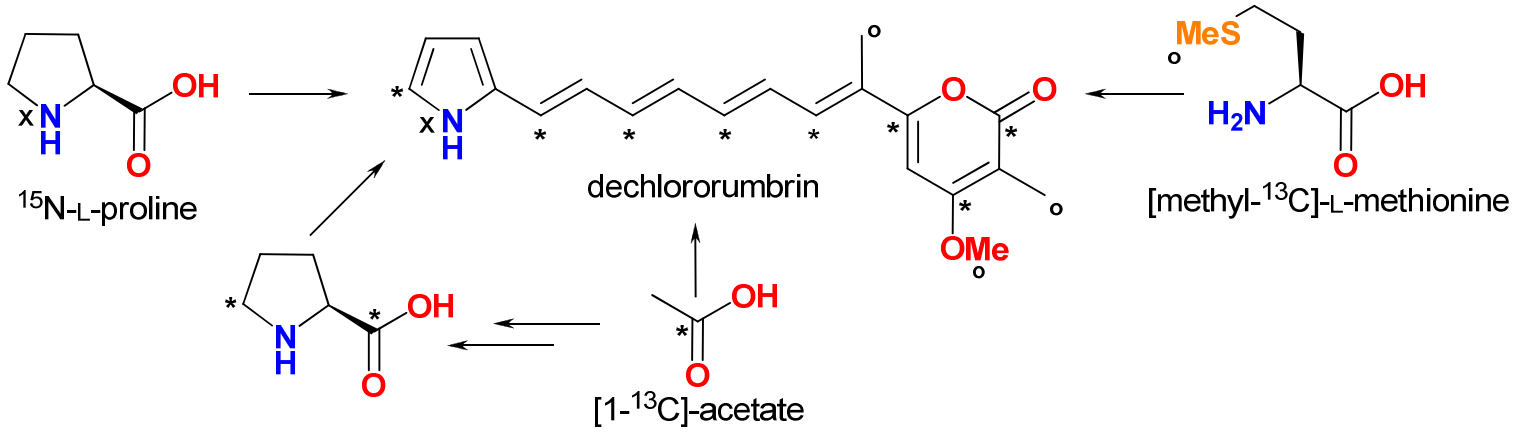


homostypohydroperoxide

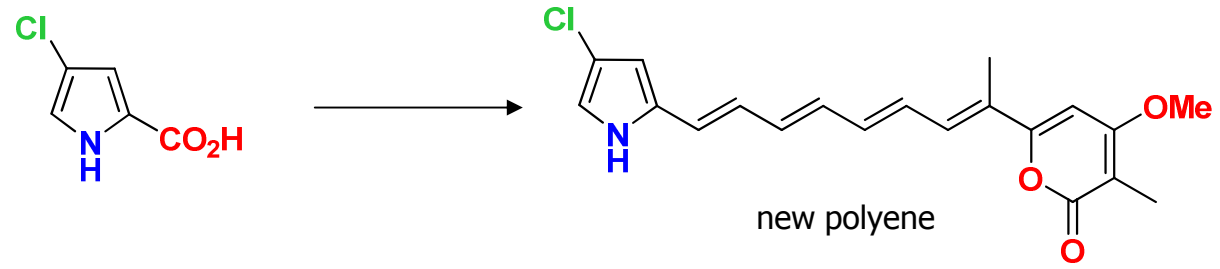
Clark, B. R. and Gerwick, W. H. *J. Nat. Prod.* **2009.** In Preparation.

Rumbrin Biosynthesis

- Rumbrin is an anticancer polyene from fungi
  - Atoms originate from acetate, proline, and methionine



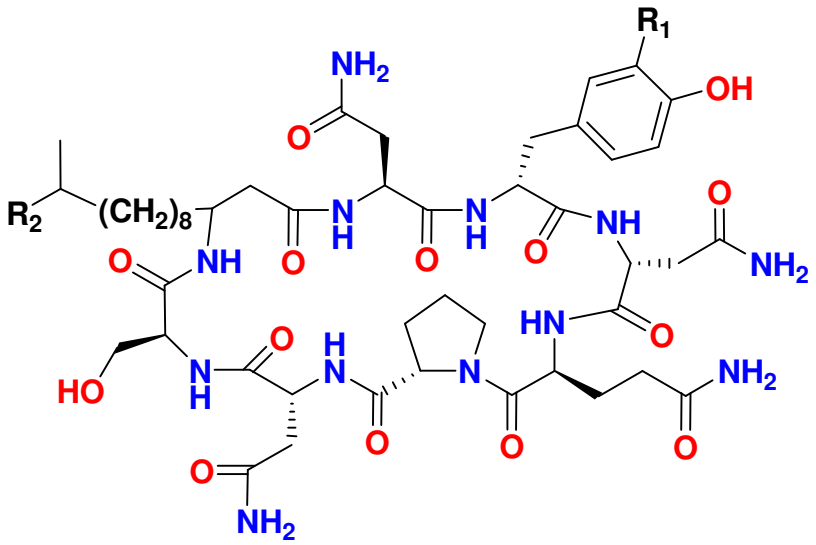
  - "unnatural" pyrrolecarboxylates accepted as substrates



Clark, Benjamin R.; Murphy, Cormac D. *Org. Biomol. Chem.* **2009**, *7*, 111-116.

Fluoroiturins

- Iturin is an antifungal peptide from bacteria
  - *Bacillus subtilis* CS93 can incorporate fluorotyrosine into iturin
  - Fractionation by HPLC yields purified fluoroiturins
  - NMR studies confirm presence of fluorotyrosine (δ_F -136.7 ppm)



Iturin (C-14)	R1 = H, R2 = H
Iturin (C-15)	R1 = H, R2 = Me
Fluoroiturin (C-14)	R1 = F, R2 = H
Fluoroiturin (C-15)	R1 = F, R2 = Me

Moran, S. *et. al. Org. Biomol. Chem.* **2009**, DOI: 10.1039/b816345f

Projects and Resources

- Proposed Projects:
  - Natural products chemistry/Drug discovery
  - Monitoring/quantifying metabolites and toxins
  - Haloperoxidase production

- Tools/expertise available
  - Chromatography – HPLC, LCMS, GCMS
  - Spectroscopy – NMR, MS
  - Biochemistry – haloperoxidases
  - Microbiology – antibacterial assays

Dr Cormac Murphy