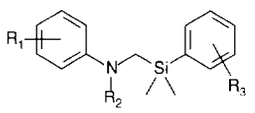
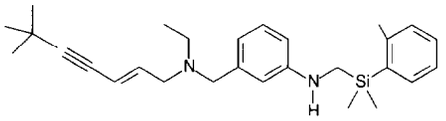
based hypocholesterolemic agents **5**, which have antioxidant properties. They also describe the synthesis and biological evaluation of **6**, which has antioxidant properties and inhibits the biosynthesis of cholesterol through inhibition of the enzyme squalene epoxidase.



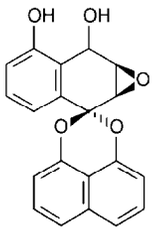
**5**



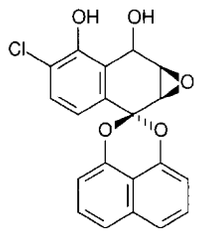
**6**

## Novel fungal phospholipase D inhibitors

Chu, M. and coworkers [*Bioorg. Med. Chem. Lett.* (1996) 6, 579–584] describe the isolation of novel phospholipase D inhibitors **7** and **8** from the fermentation broth of an unidentified fungus collected from the dead leaves of *Ruercus virginana*. Both compounds exhibited *in vitro* inhibitory activity in a phospholipase assay with $IC_{50}$ values of 24 and 19 μM respectively.



**7**

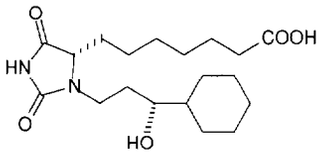


**8**

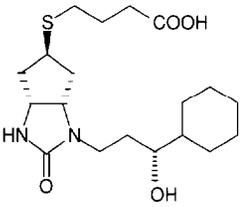
## Selective $PGD_2$ receptor agonists

Prostaglandin $D_2$ ($PGD_2$) is a potent inhibitor of human platelet aggregation, and agonists at the $PGD_2$ receptor may be useful in preventing arterial thrombosis. Although the $PGD_2$ agonist **9** has been studied in human volunteers, the clinical use of this agent is limited by its short half-life and vasodepressor side-effects. Barraclough, P. and coworkers [*Bioorg. Med. Chem.* (1996) 4, 81–90] describe the use of **9** as a lead compound in the development of selective ligands as platelet-selective agonists.

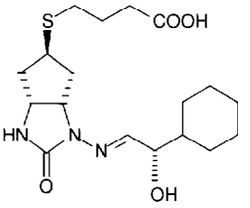
These studies identified three bicyclic imidazolidinone analogues **10**, **11**, **12** which were potent inhibitors of human platelet aggregation and selective $PGD_2$ agonists in washed platelet and jugular vein isolated tissue assays.



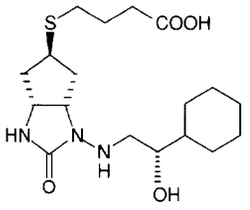
**9**



**10**



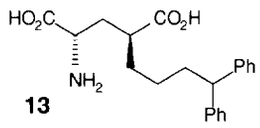
**11**



**12**

## Metabotropic glutamate receptor antagonist

The study of the G protein-linked metabotropic glutamate receptors (mGluRs) has been hindered by a lack of potent and selective antagonists. These receptors are coupled to a range of secondary messengers through adenylate cyclase inhibition, phosphoinositide-specific phospholipase C activation and modulation of ion channels. Wermuth, C.G. and coworkers [*J. Med. Chem.* (1996) 39, 814–816] have identified (2*S*,4*S*)-2-amino-4-(4,4-diphenyl-but-1-yl)-pentane-1,5-dioic acid **13** as a potent, selective antagonist of the group-2 mGluRs, which are negatively coupled to adenylate cyclase without exerting any effect on the other subclasses of receptors.



**13**

## VanX inhibitors

Clinical vancomycin resistance represents a significant problem in the treatment of Gram-positive bacterial infection. It has been previously shown that VanX, a zinc-dependent dipeptidase, is essential for vancomycin resistance in *Enterococcus faecium* [Wu, Z., Wright, G. and Walsch, C. *Biochemistry* (1995) 3, 2455–2463]. An effective design of zinc peptidase inhibitors is to use a mercaptan moiety as a zinc-binding ligand. Wu, Z. and Walsch, C. [*J. Am. Chem. Soc.* (1996) 118, 1785–1786] describe an investigation into the use of dithiol compounds as potent, time-dependent inhibitors of VanX. Of the compounds evaluated, 2,3-dimercapto-1-propanesulphonic acid and 2,3-dimercapto-1-propanol were found to be the most potent. The authors suggest that the incorporation of the dithiol moiety into the natural VanX D-Ala-D-Ala substrate scaffold may yield a more potent and specific inhibitor of VanX, which could be used to overcome the vancomycin resistance of Gram-positive bacteria.