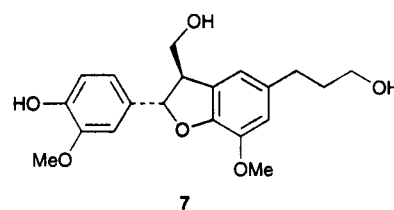
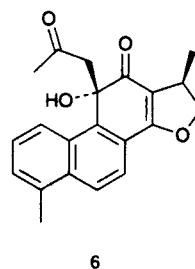
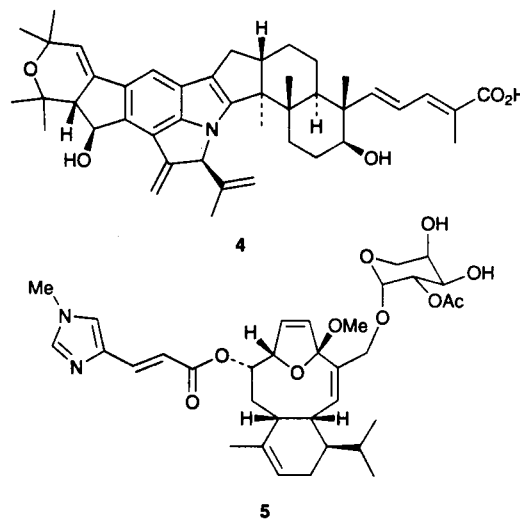
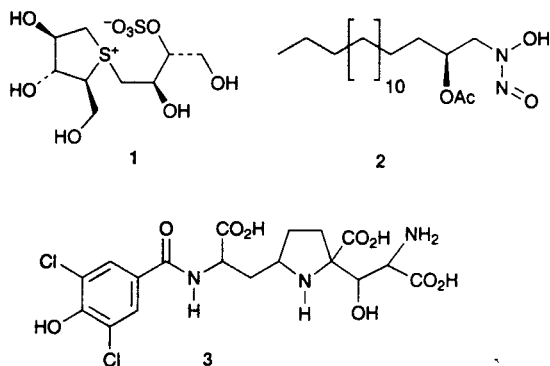


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A potent α -glycosidase inhibitor, salacinol **1**, has been isolated from an antidiabetic Ayurvedic tradition medicine, *Salacia reticulata* (M. Yoshikawa *et al.*, *Tetrahedron Lett.*, 1997, 38, 8367). The structure of salacinol **1** was confirmed by X-ray analysis. A new free radical scavenger, poecillanosine **2**, isolated from the marine sponge *Poecillastra* spec. aff. *tenuilaminaris* during screening for inhibitors of lipid peroxidation, contains the rare nitrosohydroxyalkylamine functionality (T. Natori *et al.*, *Tetrahedron Lett.*, 1997, 38, 8349). Kaitocephalin **3**, a metabolite of *Eupenicillium shearii*, is a glutamate receptor antagonist (K. Shin-ya *et al.*, *Tetrahedron Lett.*, 1997, 38, 7079).

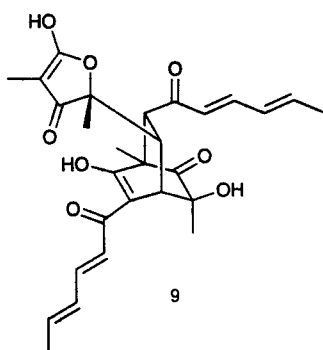
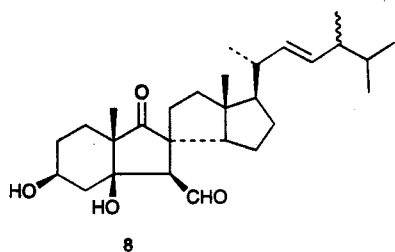


The structure of the potent insecticide, nodulisporic acid **4** from a *Nodulisporium* sp., was determined by extensive NMR analysis and confirmed by a crystal structure determination of a derivative (J. G. Ondeyka *et al.*, *J. Am. Chem. Soc.*, 1997, 119, 8809). Eleutherobin **5**, a eunicellane glycoside from an *Eleutherobia* species, shows **microtubule stabilizing properties similar to Taxol[®]** (W. Fenical and co-workers, *J. Am. Chem. Soc.*, 1997, 119, 8744). The total synthesis of eleutherobin **5** has been carried out by K. C. Nicolaou and co-workers (*Angew. Chem.*, 1997, 109, 2630). Danshenol A **6**, from the root of *Salvia miltiorhiza*, is an aldol adduct of acetone and dihydro-tanshinone I (S. Kadota and co-workers, *Chem. Pharm. Bull.*, 1997, 45, 1306). Danshenol A **6** inhibits aldose reductase.

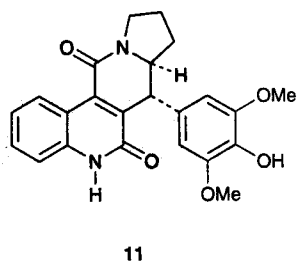
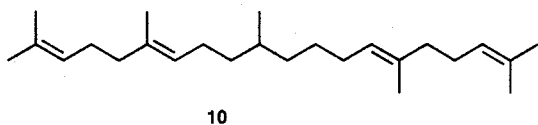
The structures of several 8-5' neolignans have been revised from the *cis* to the *trans* configuration, such as **7**, on the basis of ¹H NMR characteristics of synthetic compounds (A. F. A. Wallis and co-workers, *Phytochemistry*, 1997, 46, 929). There is no evidence for the natural occurrence of any *cis* 8-5' neolignans so far. V. S. Parmar *et al.* have reviewed the secondary metabolites obtained from the genus *Piper* over the past 90 years (*Phytochemistry*, 1997, 46, 597). They report that of the 700 species belonging to this genus only 84 have been examined and have provided 592 different compounds. In a challenging paper G. Guella *et al.* attempt to classify red seaweeds in the genus *Laurencia* into four lineages according to the stereochemical features of their metabolites (*Tetrahedron Lett.*, 1997, 38, 8261). It is true that there appears to be a relationship between the stereochemistry of the metabolites

found in any particular morphologically homogeneous collection of *Laurencia*. However there are problems with the assignment of the absolute configuration of metabolites such as the chamigrane sesquiterpenoids. Reconsideration should be given to the classification of metabolites using stereochemical descriptors which change with different substituents in the metabolites and test ones understanding of the Cahn-Ingold-Prelog rules.

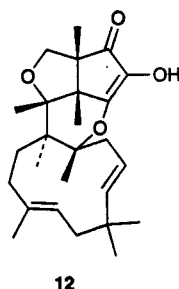
Citreospirosteroid **8** is a metabolite of a hybrid strain derived from *Penicillium citreo-viride* (S. Kosemura *et al.*, *Tetrahedron Lett.*, 1997, 38, 7373). M. Satake and co-workers have isolated trichotetronine **9** from a *Trichoderma* species (*J. Chem. Soc., Perkin Trans. 1*, 1997, 2961). Trichotetronine **9** is apparently derived from two dimethylhexaketides by a



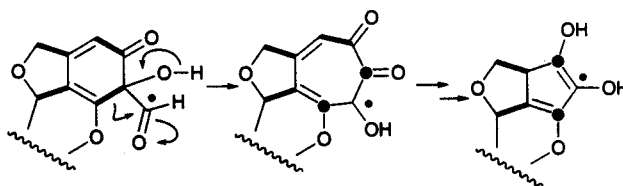
Diels–Alder reaction. An irregular acyclic sesterterpenoid, 2,6,10,15,19-pentamethylcosa-2,3,14,18-tetraene **10**, has been isolated from the methanogenic archaeon *Methanosarcina mazei* (J. S. Sinninghe Damsté *et al.*, *Tetrahedron Lett.*, 1997, 38, 6881). The sesterterpenoid **10** is presumably formed by **head to tail coupling of farnesyl diphosphate and geranyl diphosphate**. Isaindigotidione **11** from *Isatis indigotica* is the first derivative of indolizino[7,6-*c*]quinoline to be found in nature (G. Qin and co-workers, *Tetrahedron*, 1997, 53, 13 323).



Incorporation studies with ^{13}C -labelled acetates and methionine have shown that the biosynthesis of the cyclopentenone ring in xenovulene A[®] **12** from *Acremonium strictum* is intriguing (T. J. Simpson and co-workers, *Chem. Commun.*, 1997, 2245). The results are consistent with the cyclopentenone

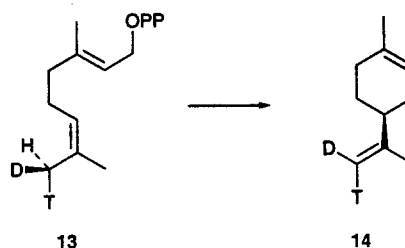


ring of xenovulene A[®] **12** being formed from a C-methylated phenolic precursor which is ring expanded to a tropolone followed by two ring contractions Scheme 1. A recombinant

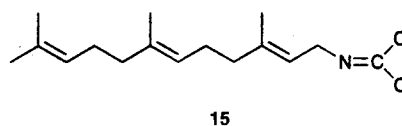


Scheme 1

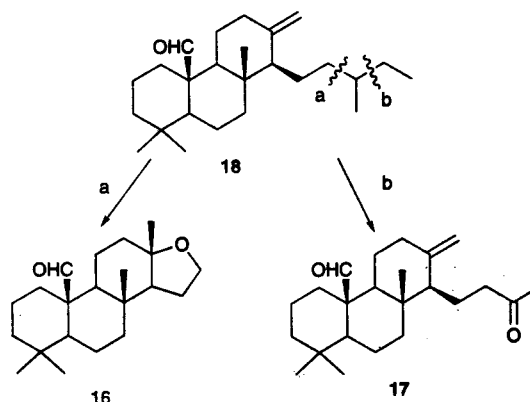
form of (4*S*)-limonene synthase from *Mentha spicata* has been used to cyclise geranyl diphosphate **13**, with a chirally labelled methyl group, to limonene **14** (R. M. Coates *et al.*, *Chem.*



Commun., 1997, 2079). The authors conclude that a *re* facial, *anti* proton elimination at the *cis* methyl group is involved in the biosynthetic pathway. The biosynthetic origin of the dichloroimine carbon of stylotellane A **15** from *Stylotella*

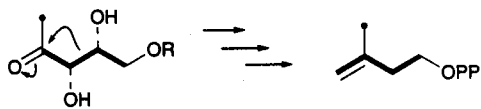


aurantium has been demonstrated by the incorporation of labelled cyanide (M. J. Garson and co-workers, *Tetrahedron Lett.*, 1997, 38, 7947). Stable isotope incorporation studies using acetate and mevalonolactone are consistent with the hypothesis that cadlinaldehyde **16** and luteone **17** are derived by cleavage of a sesterterpenoid such as **18** by the dorid



nudibranch *Cadlina luteomarginata* (R. J. Anderson and co-workers, *J. Org. Chem.*, 1997, 62, 7239).

The biosynthetic incorporation of [1-¹³C]- and [2,3,4,5-¹³C₄]-1-deoxy-D-xyulose into β-carotene, lutein, phytol and sitosterol in cultures of *Cantharanthus roseus* has been studied by D. Arigoni *et al.* (*Proc. Natl. Acad. Sci. USA*, 1997, 94, 10 600). The pattern of incorporation conclusively showed that 1-deoxy-D-xyulose, and not mevalonate, is the precursor of phytol, β-carotene and lutein. There was also minor diversion of the label into the phytosterols (6%). The work also showed conclusively that the rearrangement to give the isopentenyl pyrophosphate is exclusively intramolecular (Scheme 2).

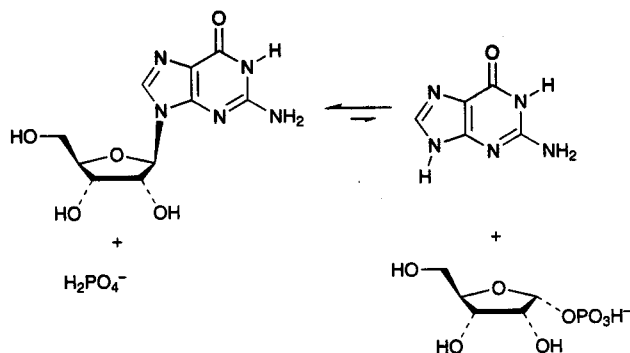


Scheme 2

Reviews of the biosynthesis of Taxol[®] have been presented by M. Hezari and R. Croteau (*Planta Med.*, 1997, 63, 291) and J. Rohr (*Angew. Chem., Int. Ed. Engl.*, 1997, 36, 2190). The incorporation of [1,2-¹³C₂]acetate gives a labelling that is consistent with Taxol[®] being a terpene derived from the non-mevalonate pathway. The biosynthesis and metabolism of the asparatate derived amino acid in plants has been reviewed (P. J. Lea and co-workers, *Phytochemistry*, 1997, 46, 395).

The controversy over the existence of so called 'low-barrier hydrogen bonds' continues to provoke both experimentation and discussion. E. L. Ash *et al.* have carried out extensive NMR studies on the catalytic triad of a serine protease, which is one of the more commonly cited examples of a system where a low-barrier hydrogen bond may occur (*Science*, 1997, 278, 1128). They conclude from their studies on α-lytic protein that there is **no evidence for the proposed 'special' hydrogen bond**; the discussions will no doubt continue. The first high quality X-ray crystal structure of a NO generating enzyme has been reported (B. R. Crane *et al.*, *Science*, 1997, 278, 425). The structure of the NO synthase oxygenase domain shows an unusual fold, resembling a baseball glove, in the palm of which sits the active site heme. The positioning of the hydrophobic oxygen binding pocket and the polar arginine binding pocket can be clearly seen, which will form a useful template for the design of inhibitors. Consecutive papers give a detailed structural and mechanistic picture of the six electron reduction of sulfite to sulfide, and nitrite to ammonia, by the *Escherichia coli* sulfite reductase hemoprotein (B. R. Crane *et al.*, *Biochemistry*, 1997, 36, 12 101 and 12 120).

An extensive study of human purine nucleotide phosphorylase, which catalyses the formation of purine nucleosides from the free base and ribose-1-phosphate (Scheme 3), has been



Scheme 3

reported by the group of M. D. Erion in three consecutive papers (*Biochemistry*, 1997, 36, 11 725, 11 735 and 11 749). The studies include structure-function analysis using site directed mutagenesis and steady state kinetics, X-ray crystallographic and modelling studies to determine the catalytic mechanism, which appears to be *via* an oxocarbenium ion, and site directed mutagenesis to reverse the substrate specificity from 6-oxo- to 6-amino-purines while still maintaining a high degree of catalytic efficiency. FTIR has been used to quantify the α-helix and β-sheet content of subtilisin Carlesberg dissolved in aqueous and non-aqueous solvents, and this has been related to the activity of the dissolved enzyme (K. Xu *et al.*, *Biotech. Bioeng.*, 1997, 56, 485). While previous findings showed no correlation for suspended enzymes, the dissolved enzyme activity is maximum in non-aqueous solvents when the α-helix and β-sheet content is identical to that in the aqueous solution.

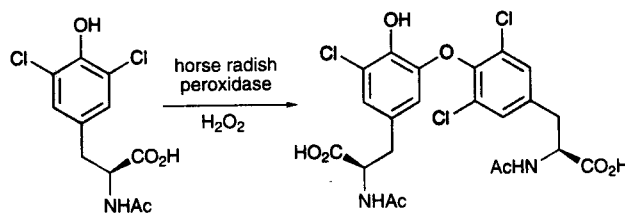
The isolation of an (*S*)-hydroxynitrile lyase and its three dimensional crystal structure has recently been reported (H. Greiengl *et al.*, *Chem. Commun.*, 1997, 1933). This is complementary to the *R* specific lyase isolated from almonds and the synthetic utility of these enzymes is outlined in the paper (Scheme 4). A mild method for carrying out the phenolic



X = H or R²

Scheme 4

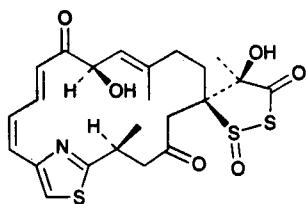
coupling of halogenated tyrosine derivative (Scheme 5) using horse radish peroxidase in the presence of hydrogen peroxide may well prove to be a powerful synthetic tool (Z.-W. Guo



Scheme 5

et al., *J. Org. Chem.*, 1997, 62, 6700). The use of peroxidases in the catalysis of selective oxidations has been comprehensively reviewed by R. Sheldon and co-workers (*Tetrahedron*, 1997, 53, 13 183). A review of the synthetic utility of epoxide hydrolases in the generation of chiral vicinal diols and other chiral molecules has recently been published (I. V. J. Archer, *Tetrahedron*, 1997, 53, 15 617). The review includes details of the reaction mechanisms of a range of epoxide hydrolases and the nucleophiles that have been used, and contains information on the substrates that are accepted and the stereochemistry and regiochemistry of the products formed.

The *de novo* design of proteins moved a step closer with a publication on the fully automated computer design and experimental validation of a novel sequence of an entire protein designed to adopt a particular fold (B. I. Dahiya and S. L. Mayo, *Science*, 1997, 278, 82). A library of 1.9×10^{27} possible sequences designed to give a ββ motif were screened



19

in silico, and a compact, well ordered and stable protein with the desired fold which had little homology to other known sequences was isolated. A continuing study of the mode of action of the potent antitumor agent leinamycin **19** in the laboratories of K. S. Gates has shown that it can damage DNA by both alkylating the DNA and by mediating oxidative damage in the presence of thiols *via* the generation of reactive oxygen species (K. Mitra *et al.*, *J. Am. Chem. Soc.*, 1997, **42**, 11691).