Hot off the press

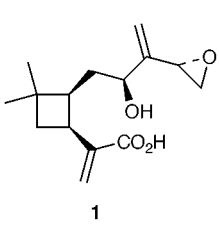
Robert A. Hill[a] and Andrew R. Pitt[b]

[a] *Department of Chemistry, Glasgow University, Glasgow, UK G12 8QQ. E-mail: bobh@chem.gla.ac.uk*
[b] *Department of Pure and Applied Chemistry, Strathclyde University, Thomas Graham Building, 295 Cathedral Street, Glasgow, UK G1 1XL. E-mail: a.r.pitt@strath.ac.uk*

Hebelophyllene F **1**, a metabolite of *Hebeloma longicaudum* is a secocaryophyllane sesquiterpenoid (W. A. Ayer and co-workers, *J. Nat. Prod.*, 1999, *62*, 484). The Formosan soft coral *Sinularia inelegans* has been found to contain the cytotoxic norditerpenoid ineleganolide **2** (G.-H. Duh, *Tetrahedron Lett.*, 1999, *40*, 6033). Ineleganolide **2** appears to be a cyclised norcembrane diterpenoid. The sesquiterpenoid sclerocarpic acid **3**, from the stem bark of *Glyptopetalum sclerocarpum*, shows antiviral activity (R. Bavovada and co-workers, *Planta Med.*, 1999, *65*, 257). Sclerocarpic acid **3** has some structural similarity to the diterpenoid aphidicolin, which also shows antiviral activity. A strain of *Gymnascella dankaliensis* isolated from the marine sponge *Halicondria japonica* produces a cytotoxic 13(14→8)-*abeo*-ergostane dankasterone **4** (A. Numata and co-workers. *Chem. Commun.*, 1999, 1321).

The amathaspiramides, such as amathaspiramide A **5**, are spiro-alkaloids from the marine bryozoan *Amathia wilsoni* (B. D. Morris and M. R. Prinsep, *J. Nat. Prod.*, 1999, *62*, 688). Slagenin A **6**, a metabolite of the marine sponge *Agelas nakamurai*, contains a tetrahydrofuro[2,3-*d*]imidazolidin-2-one moiety (J. Kobayashi and co-workers, *Tetrahedron Lett.*, 1999, *40*, 5709). The novel hexacyclic alkaloid, tronoharine **7**, has been isolated from the stem extract of *Tabernaemontana corymbosa* (T.-S. Kam, *Tetrahedron Lett.*, 1999, *40*, 5409). Pyrinodemin A **8**, a cytotoxic pyridine alkaloid with a *cis*-cyclopenta[*c*]isoxazolidine moiety has been isolated from the marine sponge *Amphimedon* sp. (J. Kobayashi and co-workers, *Tetrahedron Lett.*, 1999, *40*, 4819).

Haplosamate A **9**, isolated from a *Xestospongia* sp., contains a sulfamate ester and shows inhibition of HIV-1 integrase (A. Qureshi and D. J. Faulkner, *Tetrahedron*, 1999, *55*, 8323). Hairy root cultures of *Lithospermum erythrorhizon* produce rhizonone **10** which is probably derived biosynthetically from geranylhydroquinone **11** (H. Fukui *et al.*, *Phytochemistry*, 1999,



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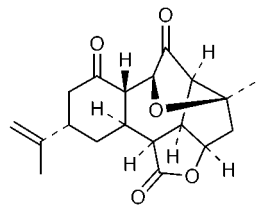

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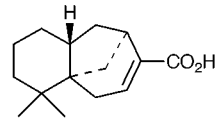

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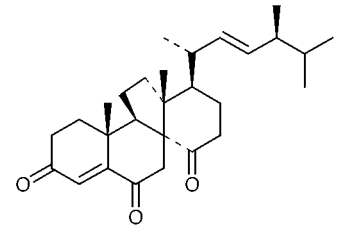

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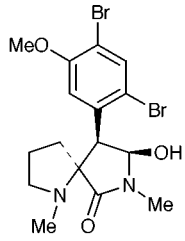

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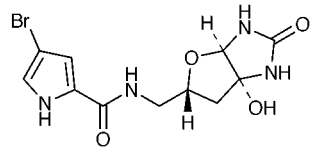

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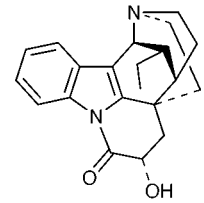

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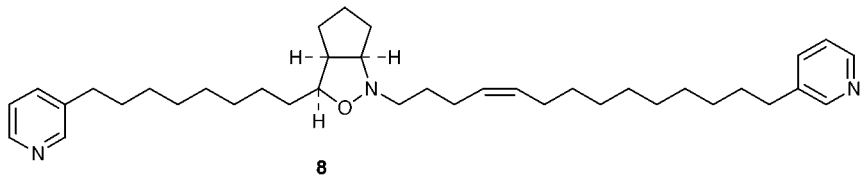

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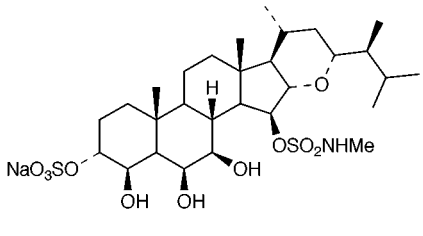

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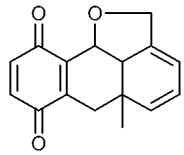

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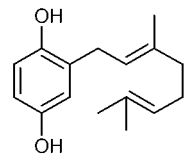

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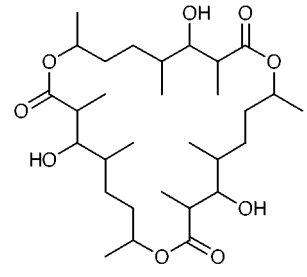

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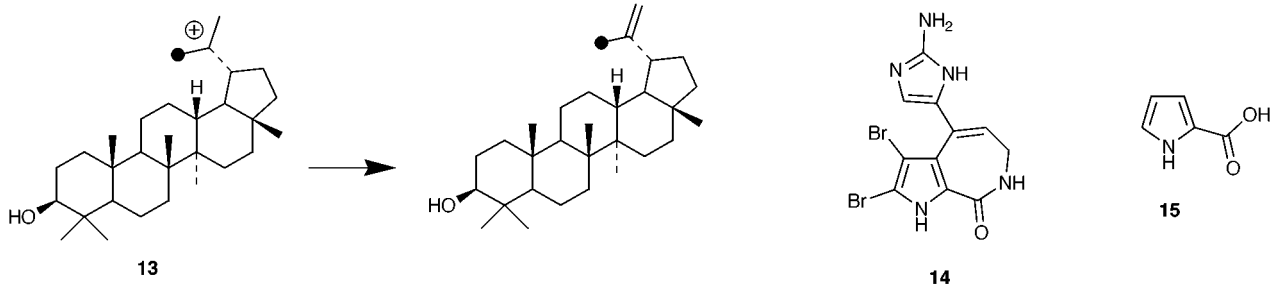
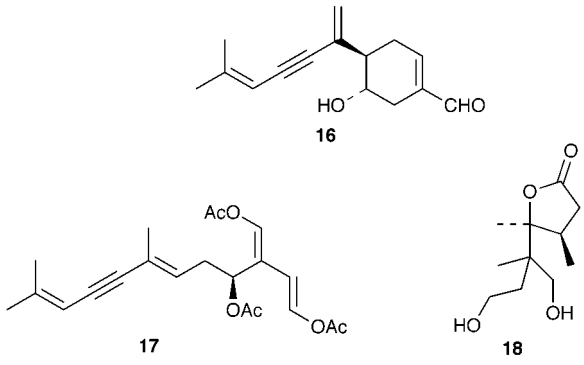


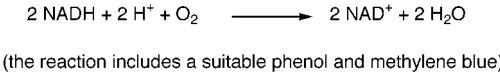
Scheme 1

51, 511). A C_3-symmetric macrolactone dasypogalactone **12** has been isolated from the Indonesian lichen *Usnea dasypoga* (K. Krohn and co-workers, *Eur. J. Org. Chem.*, 1999, 1719).

The presence of two types of lupeol synthase in plants which differ in amino acid sequence as well as deprotonation mechanism has been demonstrated by the cloning of lupeol synthases from *Olea europea* and *Taraxacum officinale*. Both synthases show only 58% amino acid sequence identity with the known *Arabidopsis thaliana* lupeol synthase. Feeding experiments have demonstrated that the two new lupeol synthases show strict discrimination by abstracting a proton from only one of the two methyl groups of the lupenyl cation **13** (Scheme 1) whereas the synthase from *Arabidopsis thaliana* abstracts a proton from both methyl groups in equal ratio (Y. Ebizuka and co-workers, *Tetrahedron Lett.*, 1999, *40*, 5553). ^{14}C-Labelling studies demonstrated that histidine but not arginine was incorporated into stevensine **14** in cell cultures of the marine sponge *Teichaxinella morchella* (P. Andrade *et al.*, *Tetrahedron Lett.*, 1999, *40*, 4775). Both ornithine and proline were also incorporated presumably *via* an intermediate such as pyrrole-2-carboxylic acid **15**. It is proposed that the unstable sesquiterpenoid metabolite volvatellin **16**, from a *Volvatella* mollusk, is derived biosynthetically from the farnesane sesquiterpenoid caulerpenyne **17** (A. Fontana *et al.*, *J. Nat.Prod.*, 1999, *62*, 931). The biosynthetic origin of ficusolide **18**, from *Ficus microcarpa*, is intriguing (Y.-H. Kuo and Y.-C. Li, *Chem. Pharm. Bull.*, 1999, *47*, 299).



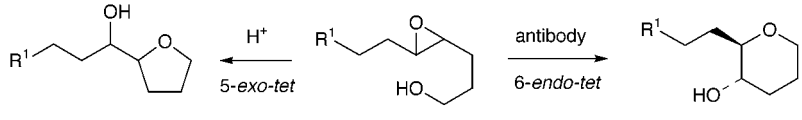
The controversial suggestion that medium to strong magnetic fields can affect enzymatic reactions has been given a boost by some recent experimental evidence (A. C. Møller and L. F. Olsen, *J. Am. Chem. Soc.*, 1999, *121*, 6351). Using the oscillating peroxidase reaction (Scheme 2) they were able to show that fields of around 3000 G were able either to affect the amplitude of the oscillations or to cause a shift of dynamics between neighbouring states. Clever engineering of the redox



Scheme 2

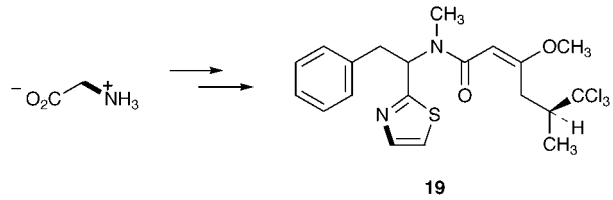
potential of the flavin cofactor and association with old yellow enzyme has caused a switch of the equilibrium of the enzyme from a reductase to a rather useful, albeit rather slow, desaturase that requires only O_2 for activity (V. S. N. Murthy *et al.*, *J. Am. Chem. Soc.*, 1999, *121*, 5344). The crystal structures of four antibodies that catalyse the disfavoured 6- and 7-*endo-tet* ring closure of an alcohol onto an epoxide (for example Scheme 3), for which there is no good chemical or enzymatic equivalent, have been solved and give some indication of the structural basis for catalysis (K. Gruber *et al.*, *Biochemistry*, 1999, *38*, 7062). The controversy over the existence of an enzyme bound intermediate in the catalytic cycle of 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase rumbles on. Careful experimental work using single turnover and low temperature kinetic methods refute previous NMR evidence of an intermediate, and identify possible structures for the compounds seen in the NMR spectrum (J. Lewis *et al.*, *Biochemistry*, 1999, *38*, 7372). Studies of the effect of pressure on the catalytic oxidation of benzyl alcohol by yeast alcohol dehydrogenase has thrown up some interesting results (Y.-K. Cho and D. B. Northrop, *Biochemistry*, 1999, *38*, 7470). The effect appears to be biphasic; at moderate pressure there is increased capture of substrate by activation of the hydride transfer step, whereas at higher pressure the enzyme appears to adopt a conformation where NAD^+ is less tightly bound. The volume change of the tighter binding of cofactor runs opposite to that of increased hydride transfer, which might not be expected if the substrate were more tightly bound in the transition state complex. Detailed kinetic, NMR, mass spectrometric and X-ray analysis of the interaction of γ-lactams whose structure is based on inhibitory β-lactams with porcine pancreatic elastase has given a mechanistic insight into how the β-lactams function as serine protease inhibitors (R. C. Wilmouth *et al.*, *Biochemistry*, 1999, *38*, 7989).

A novel method has been developed for the study of substrate channelling between *Escherichia coli* aspartate aminotransferase (ASAT) and malate dehydrogenase (MDH) that may be of wider use (M. K. Geck and J. F. Kirsch, *Biochemistry*, 1999, *38*, 7989). Inclusion in the assay of a large excess of inactive variants of ASAT that should outcompete the wild type enzyme for "docking sites" on MDH caused no change in the rate of the reaction, suggesting that there is no direct transfer of the substrate. A short review of single molecule enzymology which describes a little of the techniques that are used and the results and information that are obtained, has been published recently



Scheme 3

(X. S. Xie and H. P. Lu, *J. Biol. Chem.*, 1999, *274*, 15967). A new NMR experiment is described for the detection of intact ^{13}C–^{15}N units in biosynthetic studies (R. T. Williamson *et al.*, *Tetrahedron Lett.*, 1999, *40*, 5175). The modified GHNMBC experiment relies on the ^{1}H–^{13}C coupling of a proton attached to the carbon of the ^{13}C–^{15}N to give a clear indication of the intact unit. This method should be of wide use in biosynthetic studies but is not applicable to natural products lacking a suitably placed proton. The technique was used to confirm the cysteine origin of the thiazole ring of the cyanobacterial metabolite barbamide (**19**) using the incorporation of [2-^{13}C, ^{15}N]glycine (Scheme 4).



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Scheme 4

Three interesting reviews on the discovery, action, generation and physiological importance of nitric oxide from the Nobel prize winners F. Murad, R. F. Furchgott and L. T. Ignarro have appeared back to back and make an interesting and complete story (*Angew. Chem., Int. Ed.*, 1999, *38*, 1856, 1870 and 1882 respectively). Another review on NO, focussing more on the chemistry, also appeared recently (S. Pfeiffer *et al.*, *Angew. Chem., Int. Ed.*, 1999, *38*, 1714). A review of the role of metals in medicine, such as in anticancer, NMR imaging, radiodiagnostics and therapeutics and a host of other applications has appeared recently (Z. Guo and P. J. Sadler, *Angew. Chem., Int. Ed.*, 1999, *38*, 1512). A wide ranging review of sphingolipid metabolic pathways and their role in neurodegenerative diseases covering structure, function, regulation and inhibition of biosynthesis, catabolism, pathobiochemistry and therapy has appeared recently (T.Kolter and K. Sandhoff, *Angew. Chem., Int. Ed.*, 1999, *38*, 1532).