Hot off the press

Robert A. Hill and Andrew Sutherland

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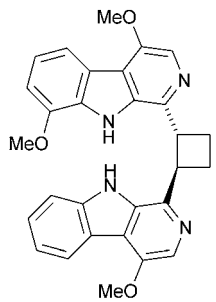
A personal selection of 29 recent papers is presented covering various aspects of current developments in bioorganic chemistry and novel natural products such as closthioamide from the anaerobic bacterium *Clostridium cellulolyticum*.

The biosynthetic origin of a cyclobutane ring in a natural product often provokes interesting questions. Quassidine A **1**, from *Picrasma quassioides*, is the first bis-β-carboline alkaloid with a cyclobutane ring (X.-S. Yao and co-workers, *J. Nat. Prod.*, 2010, *73*, 167). Two possible pathways for the formation of the cyclobutane ring are proposed by the authors. Phantasmidine **2** has been isolated from the skin of the Ecuadorian poison frog *Epipedobates anthonyi* (R. W. Fitch *et al.*, *J. Nat. Prod.*, 2010, *73*, 331). The authors suggest that the cyclobutane ring is formed by rearrangement of the co-occurring epibatidine **3** or a common precursor.



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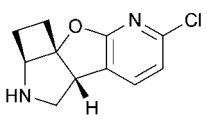

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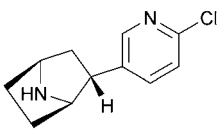

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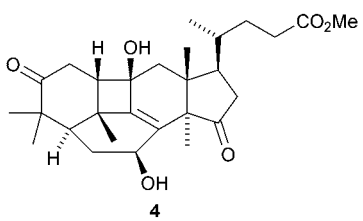
The fruiting body of *Ganoderma sinense* is the source of methyl ganosinensate A **4**, whose structure was confirmed by X-ray analysis (M.-H. Qiu and co-workers, *Org. Lett.*, 2010, *12*, 1656). Methyl ganosinensate A **4** is a 1,11-cyclised norlanostane triterpenoid, and a possible pathway for the cyclisation is proposed. Plumisclerin A **5**, from the soft coral *Plumigorgia terminosclera*, is a xenicane diterpenoid with C1–C5 and C6–C19 cyclisations producing a cyclobutane ring (R. Reyes and co-workers, *Org. Lett.*, 2010, *12*, 912). The cyclobutane ring of ioniol I **6**, from the red alga *Spaerococcus coronopifolius*, is thought to arise by cyclisation of bromosphaerol **7** (V. Roussis and co-workers, *Chem. Biodiversity*, 2010, *7*, 666). A biosynthetic pathway to the co-occurring ioniol II **8** is also proposed.



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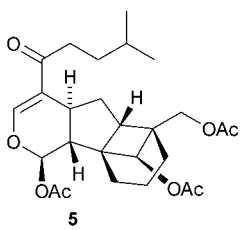

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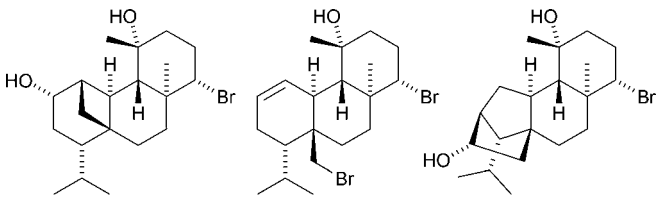
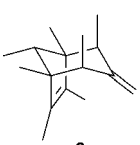
Department of Chemistry, Glasgow University, Glasgow, G12 8QQ, UK. E-mail: andrews@chem.gla.ac.uk



6 **7** **8**

The main component of the volatiles produced by the rhizobacterium *Serratia odorifera* is the highly methylated bicyclo-[3.2.1]octane derivative sodorifen **9** (W. Francke and co-workers, *Angew. Chem., Int. Ed.*, 2010, *49*, 2009). The structure of sodorifen **9** was confirmed by synthesis. Preliminary labelling studies using [2-^{13}C]acetate did not provide conclusive results about the biosynthetic origin of sodorifen **9**. Plants of the genus *Swertia* are a rich source of secoiridoids. *Swertia mileensis* produces a range of bis-secoiridoids including swerilactones E **10** and G **11**, whose structures were confirmed by X-ray analysis (J.-J. Chen and co-workers, *Tetrahedron Lett.*, 2010, *51*, 2483). The rearrangements involved in the biosynthesis of these aromatised derivatives are intriguing.



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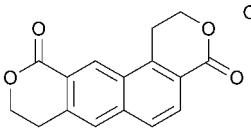

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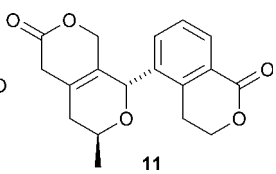

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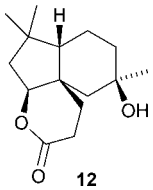
The first clovane sesquiterpenoids to be found in marine organisms, rumphellclovane A **12** and its probable biosynthetic precursor 2β-hydroxyclovan-9-one **13**, have been found in the gorgonian coral *Rumphella antipathies* (P.-J. Sung and co-workers, *Tetrahedron Lett.*, 2010, *51*, 2734). It is proposed that cosmosoic acid **14**, from the South American plant *Cosmos sulfureus*, is formed by a pinacol rearrangement of a cadinane sesquiterpenoid (*Helv. Chim. Acta*, 2010, *93*, 753). An extensive review on the chemistry and biology of the quadrane sesquiterpenoids, such as quadrone **15**, has been published (M. Presset *et al.*, *Eur. J. Org. Chem.*, 2010, 2247). Trichiliton A **16**, from *Trichilia connaroides*, is a rearranged limonoid with a [5.2.1]bicyclodecane ring system (X. Fang *et al.*, *Eur. J. Org. Chem.*, 2010, 1381). The authors propose a biosynthetic route to trichiliton A **16** from a mexicanolide-type precursor.



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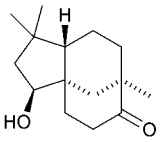

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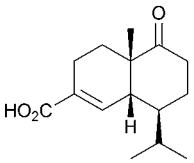

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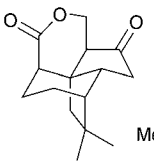

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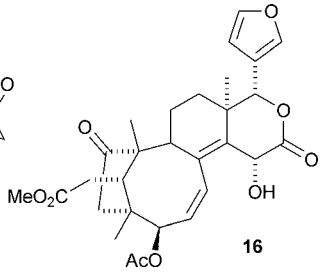

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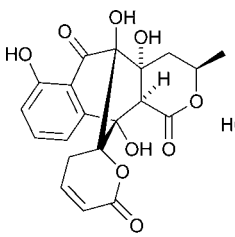
An actinomycete of the genus *Nocardiopsis*, isolated from an alkaline soil sample (pH 10) from the Datun tin mine tailings area, produces the metabolite naphthospironone A **17**, with an unusual spiro-bicyclo[3.2.1]octane–pyranone ring system (Z.-G. Ding *et al.*, *Chem. Eur. J.*, 2010, *16*, 3902). The structure of naphthospironone A **17** was confirmed by X-ray analysis. A metabolite of the anaerobic bacterium *Clostridium cellulolyticum* has been identified as the polythioamide closthioamide **18** (C. Hertweck and co-workers *Angew. Chem., Int. Ed.*, 2010, *49*, 2011). Closthioamide **18** has six thioamides in a symmetrical structure and shows interesting antibiotic properties.



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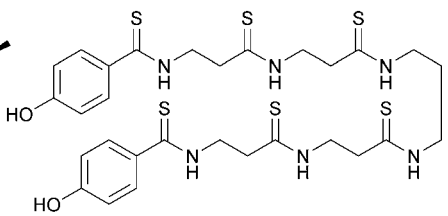

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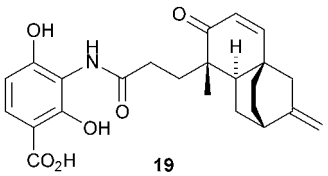
B. Shen and co-workers have studied the biosynthesis of the antibiotic platencin **19** in *Streptomyces platensis* MA7339 (*Org. Lett.*, 2010, *12*, 1744). They found that inactivation of *ptnR1*, a GntR-like transcriptional regulator, generated an engineered strain which overproduces **19** by ~100 fold and accumulates eight new congeners, platencins A_2–A_9. The antibacterial activity of the new compounds was evaluated, providing insight into the structure–activity relationship of this class of natural products. H.-W. Liu and co-workers have identified the three genes responsible for the permethylation of the rhamnose moiety in the polyketide-derived macrolide spinosyn A **20** produced by *Saccharopolyspora spinosa* (*J. Am. Chem. Soc.*, 2010, *132*, 2901). Reconstitution of the biosynthetic pathway using purified enzymes allowed elucidation of the methylation sequence.



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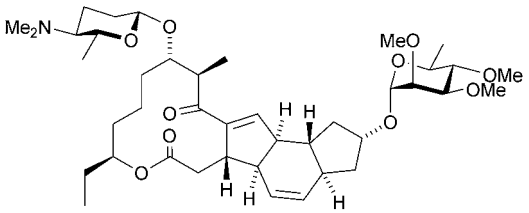

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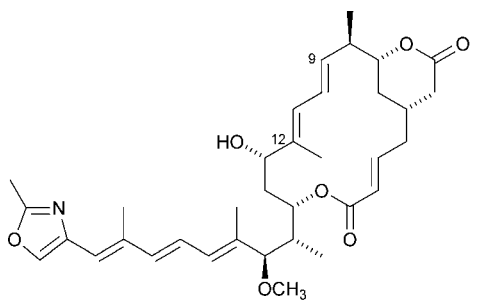
During their studies on the biosynthesis of the polyketide rhizoxin D **21** in *Burkholderia rhizoxinica*, C. Hertweck and co-workers have shown that the diene moiety (C9–C12) is formed by two consecutive α,β → β,γ double-bond shifts (*Angew. Chem. Int. Ed.*, 2010, *49*, 1460). The sequential shift is carried out by two distinct polyketide synthase (PKS) modules, one of which contains a novel dehydratase type domain. Similarly, J. Piel and co-workers have shown that a β,γ-dehydration is carried out by a *trans*-acyltransferase polyketide synthase to generate the unusual β,γ-type unsaturation found in the C3–C8 region of the polyketide bacillaene **22** (*Angew. Chem., Int. Ed.*, 2010, *49*, 1465).

The biosynthetic origin of the food-related toxin bongkrekic acid **23** from *Burkholderia gladioli* has been established (B. Rohm *et al.*, *Org. Biomol. Chem.*, 2010, *8*, 1520). Feeding studies with



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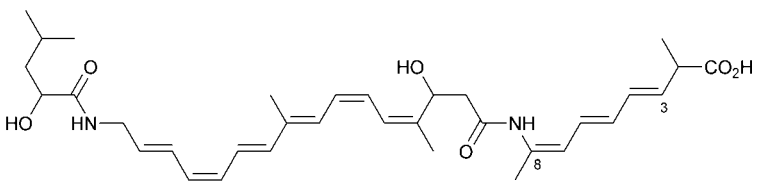

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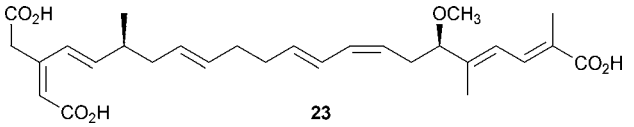

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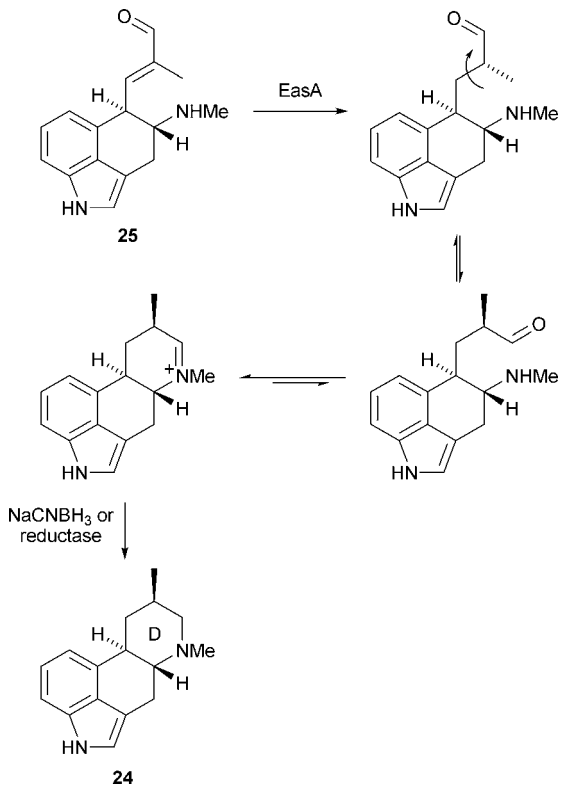
^{13}C-labelled acetates and methionine showed that **23** is a polyketide with acetate-derived β-branches and a carboxylate terminus generated from the methyl group of an acetate. A homologue of Old Yellow Enzyme encoded in the *Aspergillus fumigatus* ergot gene cluster is involved in the formation of the D-ring of festuclavine **24** (S. E. O'Connor and co-workers, *J. Am. Chem. Soc.*, 2010, *132*, 1776). The homologue enzyme EasA catalyses the reduction of the α,β-unsaturated aldehyde of chanoclavine-1 aldehyde **25** (Scheme 1). Intramolecular cyclisation, followed by reduction, completes the synthesis of the D-ring of festuclavine **24**.



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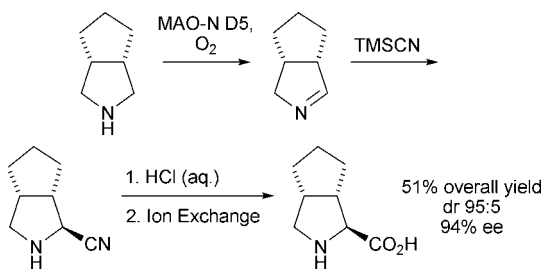
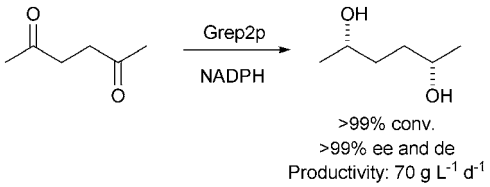
Scheme 1



Scheme 2

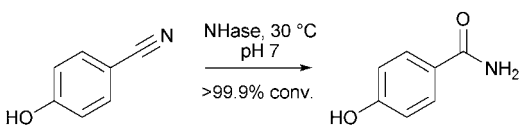


Scheme 3

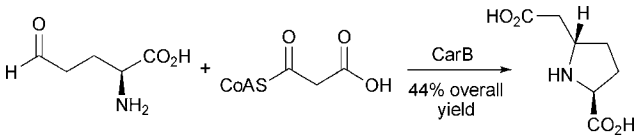
N. J. Turner and co-workers have used monoamine oxidases for the deracemisation of substituted pyrrolidines (*Angew. Chem., Int. Ed.*, 2010, *49*, 2182). Using MAO-N D5, a biocatalyst generated by directed evolution, gave imines which were then trapped with TMSCN (Scheme 2). Hydrolysis of the nitrile group allowed the isolation of proline analogues in good yields and excellent enantioselectivity. W. Hummel and co-workers have isolated and purified an enzyme from baker's yeast which is responsible for formation of the versatile building block (2*S*,5*S*)-hexanediol by reduction of 2,5-hexanedione (Scheme 3) (*Org. Biomol. Chem.*, 2010, *8*, 1540). The recombinant enzyme Grep2p demonstrated high volumetric productivity and showed catalytic activity towards other keto-compounds.

M.-J. Kim and co-workers have reviewed the recent developments in the dynamic kinetic resolution of alcohols and amines (*Eur. J. Org. Chem.*, 2010, 999). In particular, the use of one-pot metal-catalysed racemisation and enzyme acylation, as well as reactions involving precursors of alcohols and amines, are summarised. The nitrile hydratase enzyme from *Rhodopseudomonas palustris* CGA009 has been shown to hydrate a wide range of aliphatic, aromatic and heterocyclic nitriles under mild conditions with excellent chemoselectivity (Scheme 4) (J. J. Perry and co-workers, *Tetrahedron Lett.*, 2010, *51*, 1639).

C. J. Schofield and co-workers have used carboxymethylproline synthases as catalysts for the preparation of functionalised 5-, 6- and 7-membered *N*-heterocycles from amino acid aldehydes (Scheme 5) (*Chem. Commun.*, 2010, *46*, 1413). Some of the *N*-heterocycles produced from this process were also converted to the corresponding β-lactams using a carbapenem synthetase. The (*R*)- and (*S*)-enantiomers of the natural product rugulactone, an inhibitor of NF-κB activity in human lymphoma cell lines, has been prepared using an enzymatic kinetic resolution as

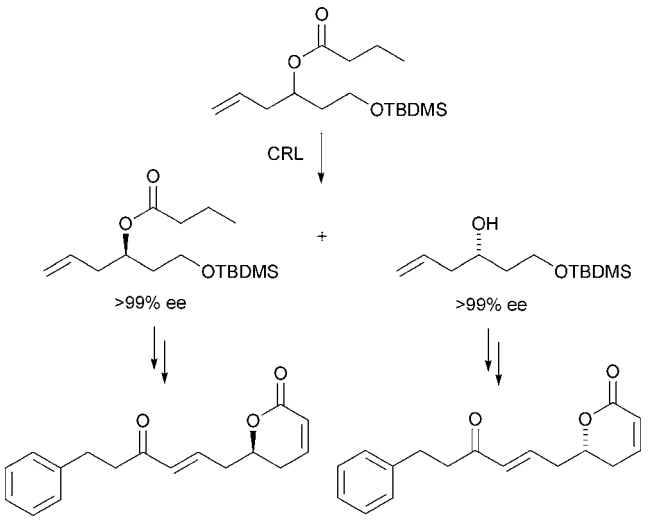


Scheme 4



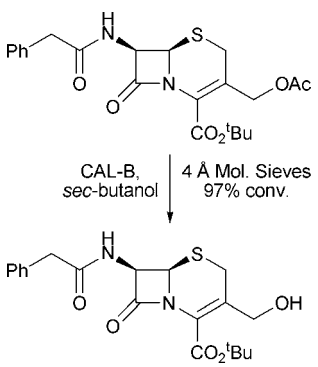
Scheme 5

the key step (N. W. Fadnavis and co-workers, *Tetrahedron: Asymmetry*, 2010, *21*, 320). Resolution of a racemic butyrate ester using *Candida rugosa* lipase gave the corresponding ester and allylic alcohol in excellent conversion and enantioselectivity, and these intermediates were then converted to (*R*)- and (*S*)-rugulactone (Scheme 6).



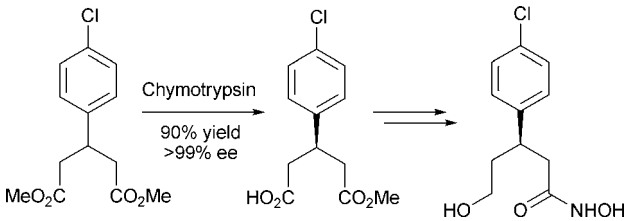
Scheme 6

L. D. Patterson and M. J. Miller have shown that *Candida antarctica* lipase B can be used for the efficient and selective hydrolysis of the 3′-hydroxymethyl position of cephalosporins (Scheme 7) (*J. Org. Chem.*, 2010, *75*, 1289). The products of this process are highly amenable to derivatisation and formation of new biologically active cephalosporin analogues. The asymmetric synthesis of new hydroxamate inhibitors of botulinum



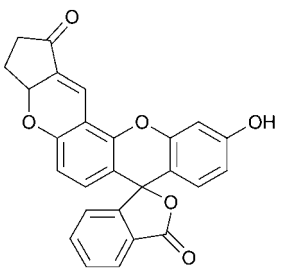
Scheme 7

neurotoxin serotype A, the most toxic protein known to man and a bioterrorism agent, has been reported (K. D. Janda and co-workers, *Org. Lett.*, 2010, *12*, 756). The key step in the synthesis of the hydroxamates involves a chymotrypsin-mediated hydrolysis, which gave the corresponding acids in excellent enantioselectivity (Scheme 8).



Scheme 8

J. Yoon and co-workers have developed a new fluorescein-base probe **26** for detecting biological thiols in aqueous solutions and cells (*Chem. Commun.*, 2010, *46*, 2751). The activity of the probe is attributed to 1,4-addition of thiols to the α,β-unsaturated ketone moiety. Its application for detecting thiols in zebrafish was also demonstrated. A two-photon fluorescent probe **27**, which is derived from a 6-dimethylamino-2-acetylnaphthalene reporter and an azathiocrown ether receptor, has been developed for the visualisation of Hg^{2+} accumulation (B. R. Cho and co-workers, *Chem. Commun.*, 2010, *46*, 2388). The probe was able to detect Hg^{2+} in live cells and fish organs at 80–150 μm depth using two-photon microscopy.



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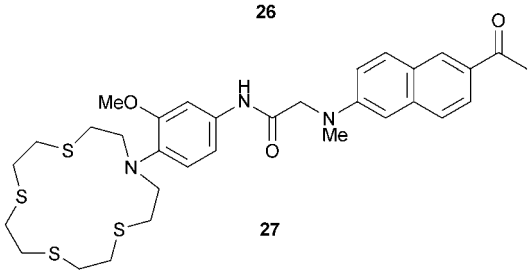

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