Hot off the press

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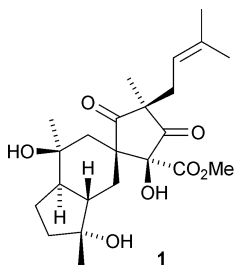
A personal selection of 30 recent papers is presented covering various aspects of current developments in bioorganic chemistry and novel natural products such as the tetrameric polysulfur dopamine-derived alkaloid lissoclibadin 8 from the ascidian *Lissoclinum* cf. *badium*.

Biyouyanagiol **1** is a acylphloroglucinol-derived constituent of the medicinal plant *Hypericum chinense* with a novel skeleton (Y. Kashiwada and co-workers, *J. Nat. Prod.*, 2009, *72*, 1447). The structure of swerilactone A **2**, from the Chinese herb *Swertia mileensis*, was confirmed by X-ray analysis (J.-J. Chen and co-workers, *Org. Lett.*, 2009, *11*, 4120). The biosynthetic origin of swerilactone A **2** is not clear from its structure.



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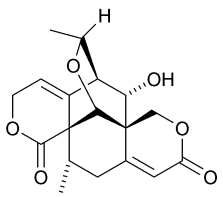

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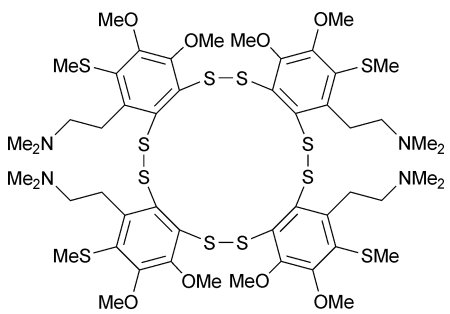
Lissoclibadin 8 **3** is a tetrameric member of a family of polysulfur dopamine-derived alkaloids from the ascidian *Lissoclinum* cf. *badium* (M. Namikoshi and co-workers, *Tetrahedron*, 2009, *65*, 9598). Naseseazine A **4**, a metabolite of a marine-derived *Streptomyces* species, has novel dimeric diketopiperazine framework (R. J. Capon and co-workers, *Org. Lett.*, 2009, *11*, 3862). The authors propose a biosynthetic pathway to naseseazine A **4** and related compounds. A biosynthetic route has been proposed for the bisindole alkaloid leucophyllidine **5**, which has been isolated from *Leuconotis griffithii* (T.-S. Kam and co-workers, *Org. Lett.*, 2009, *11*, 3962). The structure of leucophyllidine **5** was confirmed by X-ray analysis.



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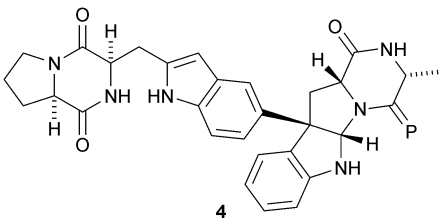

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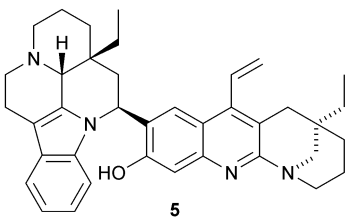

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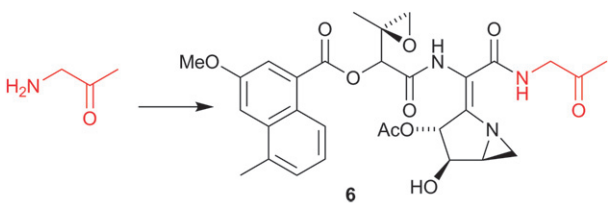
Aminoacetone has been shown to be a key precursor of the antitumour agent azinomycin A **6**, a metabolite of a *Streptomyces* species (C. M. H. Watanabe and co-workers, *Org. Lett.*, 2009, *11*, 4006). The isolation of (*Z*,*Z*)-pandanamine **7** and the corresponding (*Z*,*E*)- and (*E*,*E*)-isomers from *Stichoneuron calcicola* sheds some light on the biosynthetic origin of the *Stemona* alkaloids and suggests the reclassification of the family Stemonaceae to the order Pandanales (H. Greger *et al.*, *J. Nat. Prod.*, 2009, *72*, 1709).



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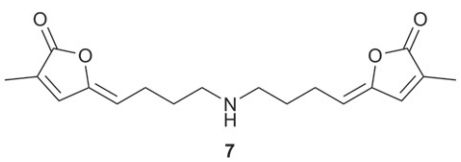

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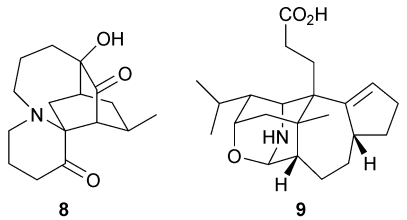
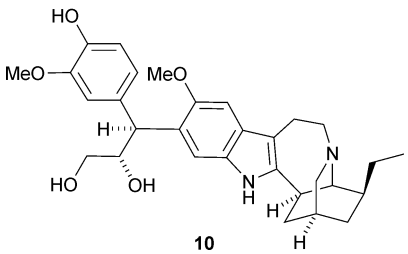
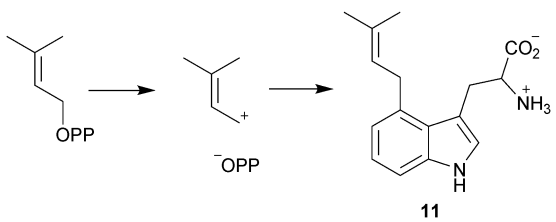
Lycopladine H **8**, from the clubmoss *Lycopodium complanatum*, has a novel skeleton including an azocane ring joined to a [2.2.2]bicyclooctane ring (J. Kobayashi and co-workers, *Tetrahedron Lett.*, 2009, *50*, 6534). A biosynthetic pathway to lycopladine H **8** *via* a phlegmarane-type precursor has been proposed. A tetracyclic alkaloid calycinumine B **9**, with an unusual

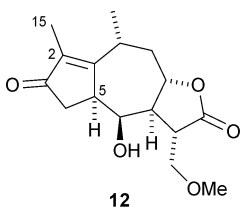
heteroatom-containing adamantane moiety, is a constituent of *Daphniphyllum calycinum* (J.-M. Yue and co-workers, *Org. Lett.*, 2009, *11*, 4692). The first iboga alkaloids with a phenylpropenoid linkage, such as conomicidine A **10**, have been isolated from *Tabernaemontana corymbosa* (K.-K. Lim and T.-S. Kam, *Helv. Chim. Acta*, 2009, *92*, 1895). The mechanism of dimethylallyltryptophan synthase has been studied, and evidence is presented that a dimethylallyl cation intermediate is involved in the biosynthesis of dimethylallyltryptophane **11** (L. Y. P. Luk and M. E. Tanner, *J. Am. Chem. Soc.*, 2009, *131*, 13932).

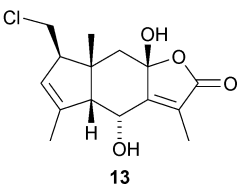




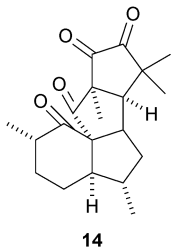


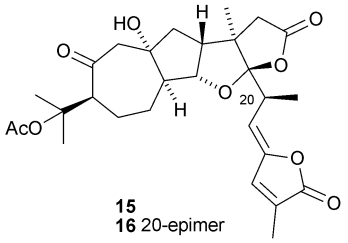
Britanlin D **12**, from *Inula britannica*, is a rearranged pseudoguaiane sesquiterpenoid (Y.-P. Shi and co-workers, *Tetrahedron Lett.*, 2009, *50*, 6315). The authors propose that britanlin D **12** is formed by 1,3-migration of the C-15 methyl group of a pseudoguaiane skeleton from C-5 to C-2. Root tubers of *Lindera aggregata* are the source of several sesquiterpenoids including linderagalactone A **13**, which has a novel rearranged eudesmane skeleton that is likely to be formed by ring-opening of a 1,3-cycloeudesmane derivative (C.-X. Zhou and co-workers, *J. Nat. Prod.*, 2009, *72*, 1497).



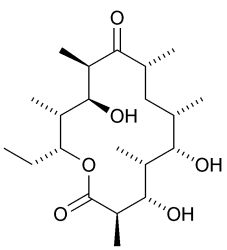


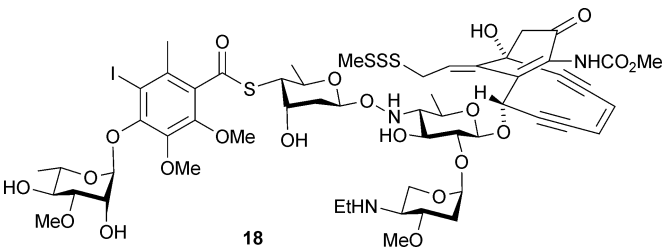
The gorgonian *Pseudopterogorgia elisabethae* continues to provide diterpenoids with interesting structures. The structure of aberrarone **14**, from this species, was confirmed by X-ray analysis and is the first example of an aberrarane skeleton (A. D. Rodriguez and co-workers, *J. Org. Chem.*, 2009, *74*, 7581). The authors propose that the aberarrane skeleton is a regular diterpene that arises by cyclisation of geranylgeranyl diphosphate. Schilancidilactones A **15** and B **16** are further examples of rearranged norcycloartanes from *Schisandra lancifolia* (H.-D. Sun and co-workers, *Tetrahedron Lett.*, 2009, *50*, 5962). The structure of schilancidilactone A **15** was confirmed by X-ray analysis.



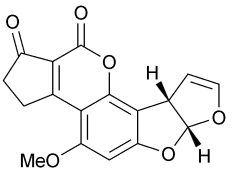


C. Khosla has provided an overview of his group's work on understanding the structures and mechanisms of polyketide synthases (PKSs) (*J. Am. Chem. Soc.*, 2009, *74*, 6416). In particular, the mechanisms of the PKSs involved in the biosynthesis of SEK4 and SEK4b as well as 6-deoxyerythronolide B **17** are described. Isolation of octaketide polyenes from *in vitro* reactions of calicheamicin PKS CalE8 and its downstream thioesterase CalE7 have called into question the previously held view that 9- and 10-membered enediynes diverge biosynthetically at the PKS stage (C. A. Townsend and co-workers, *J. Am. Chem. Soc.*, 2009, *131*, 12564). The authors propose that the biosynthesis of antitumour antibiotics such as neocarzinostatin and calicheamicin γ_1^1 **18** diverge from the action of one or more accessory enzymes working in combination with the enediyne PKS.





S. Bräse and co-workers have reviewed the chemistry and biology of mycotoxins and related fungal metabolites such as the food contaminant aflatoxin B_1 **19** (*Chem. Rev.*, 2009, *109*, 3903). S.-M. Li and co-workers have cloned, overexpressed and purified FtmOx1, a non-heme Fe(II) and α-ketoglutarate-dependent dioxygenase from *Aspergillus fumigatus* (*Org. Biomol. Chem.*,



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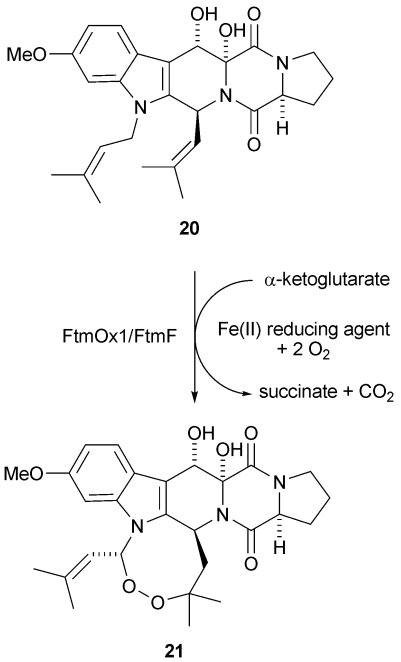
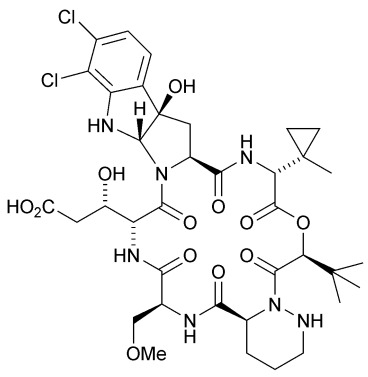
2009, *7*, 4082). FtmOx1 catalyses the conversion of fumitremorgin B **20** to the tremorgenic mycotoxin verruculogen **21** by inserting an endoperoxide bond between two prenyl moieties (Scheme 1).



Scheme 1

C. T. Walsh and co-workers have studied the two putative nonheme iron oxygenases KtzO and KtzP that are involved in the biosynthesis of the antifungal and antimicrobial kutznerides such as kutzneride 1 **22** (*J. Am. Chem. Soc.*, 2009, *131*, 13523). Recombinant expression and characterisation of these enzymes showed that they catalyse the stereospecific hydroxylation of the β-position of glutamic acid. M. T. Reetz has described the key advances in the directed evolution of enantioselective enzymes such as choosing the appropriate gene mutagenesis method and the development of high-throughput ee-screening systems (*J. Org Chem.*, 2009, *74*, 5767).



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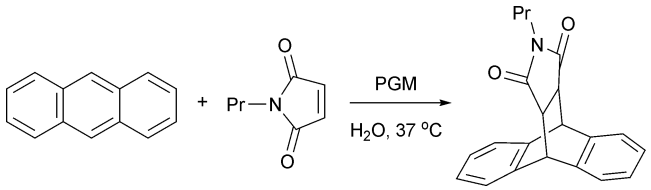
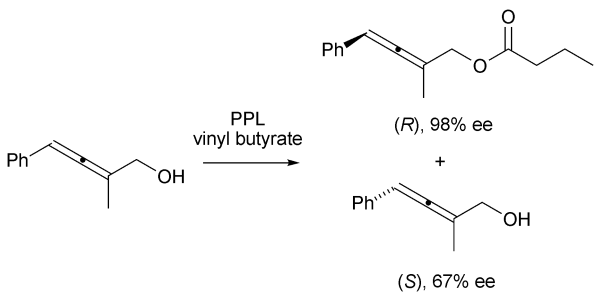
M. Gozin and co-workers have shown that organic reactions under physiological conditions can be promoted by mucin glycoproteins (*J. Am. Chem. Soc.*, 2009, *131*, 12074). For example, the Diels–Alder reaction of *N*-propylmaleimide and anthracene is accelerated by up to 200 times in the presence of porcine gastric mucin type III (PGM) compared to a reaction in standard organic solvents (Scheme 2). J. V. Comasseto and R. A. Gariani have provided a comprehensive review on the biotransformations of organic selenides and tellurides including reactions such as kinetic resolutions, oxidations and reductions (*Tetrahedron*, 2009, *65*, 8447).



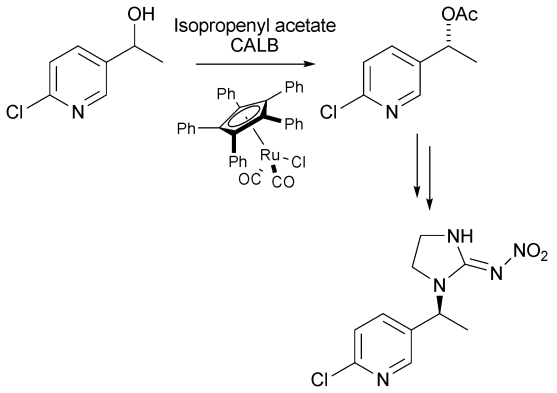
Scheme 2

J. Deska and J.-E. Bäckvall have shown that porcine pancreatic lipase can be used for the kinetic resolution of axially chiral primary allenic alcohols, providing the desired esters with excellent enantioselectivities and with *E* values above 200 (Scheme 3) (*Org. Biomol. Chem.*, 2009, *7*, 3379). The group of J.-E. Bäckvall have also described the synthesis of a neonicotinoide pesticide by using a dynamic kinetic resolution to effect the key step (*J. Org. Chem.*, 2009, *74*, 7407). Using *Candida antarctica* lipase B (CALB) and isopropenyl acetate as the acyl donor gave after optimisation the desired acetate in 91% yield and >99% ee (Scheme 4). From the acetate, a chiral chloronicotinyl insecticide, Me-imidacloprid, could be easily prepared in relatively few steps.

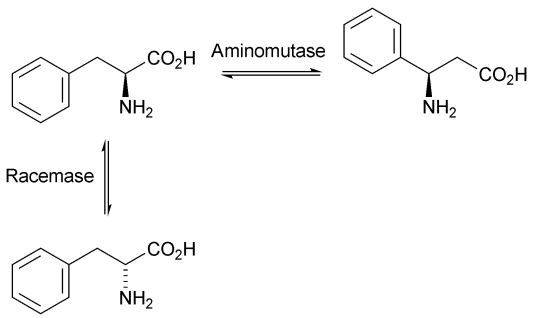


Scheme 3

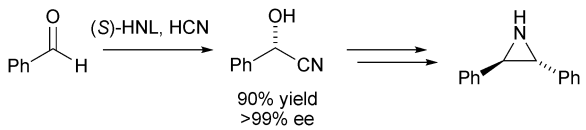
K. D. Walker and co-workers have developed a novel synthesis of (*R*)-β-arylalanines from racemic α-arylalanines using a racemase/aminomutase coupled enzyme system (Scheme 5) (*J. Org. Chem.*, 2009, *74*, 6953). The inclusion of the racemase with the aminomutase results in as much as a 19% increase in yield of the enantiopure β-arylalanines. F. P. J. T. Rutjes and co-workers have reported a mild enantioselective synthesis of *trans*-aziridines using a hydroxynitrile lyase mediated reaction for the formation of the key cyanohydrin intermediates (*J. Org. Chem.*, 2009, *74*, 7548). These were formed in excellent yields and



Scheme 4



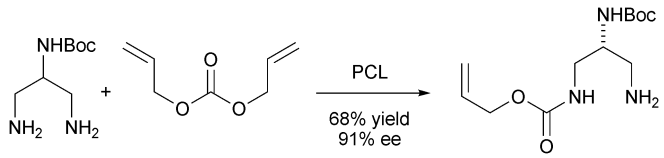
Scheme 5



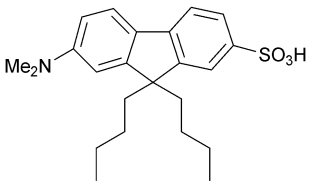
Scheme 6

enantioselectivities, and were then converted to the target *trans*-aziridines (Scheme 6).

V. Gotor and co-workers have synthesised optically active orthogonally protected polyamines using a *Pseudomonas cepacia* lipase (PCL) mediated desymmetrisation of prochiral 2-substituted-1,3-propanediamines to effect the key step (*Tetrahedron*, 2009, *65*, 8393). The substituent at the 2-position was found to have a significant influence on the stereoselectivity of the process. Ether groups at this position gave low to moderate enantioselectivities while a Boc-protected amine gave 91% ee (Scheme 7). A novel water-soluble solvatochromic fluorescent compound, 9,9-dibutyl-7-(dimethylamino)-2-fluorenesulfonate **23**, has been shown to bind to a hydrophobic site of human serum albumin (HSA) (K. K. Park and co-workers, *Org. Biomol. Chem.*, 2009, *7*, 4225). The key properties of this compound, such as high molar absorptivity and strong fluorescence, make it a potentially important probe for studying the binding properties of proteins and other biological molecules.



Scheme 7



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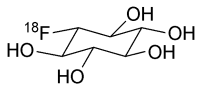
N. Vasdev and co-workers have synthesised a novel PET radiotracer, [^{18}F]-1-deoxy-1-fluoro-*scyllo*-inositol **24** (*Chem Commun.*, 2009, 5527). While this compound has low brain penetration, it shows potential in rodent tumour models for the imaging of breast cancer.



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