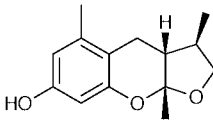
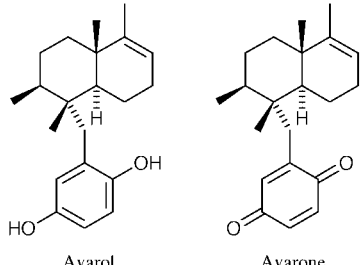
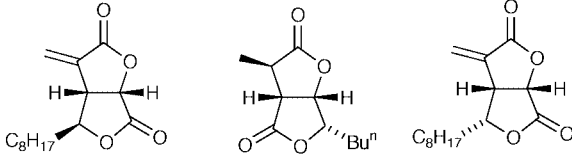
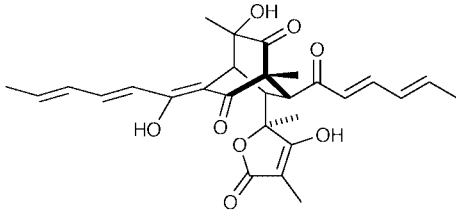
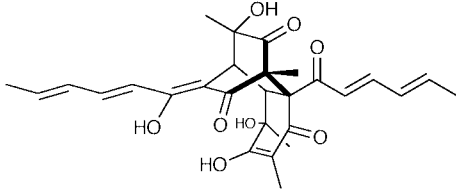
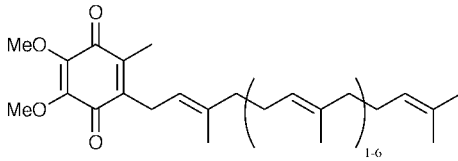
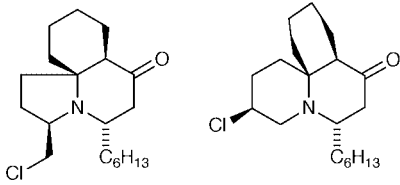
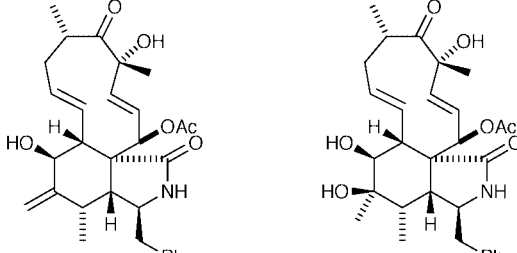
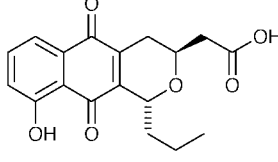
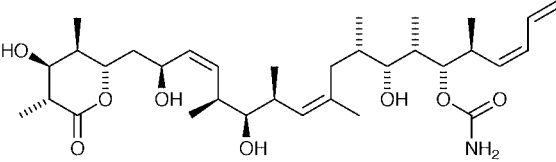
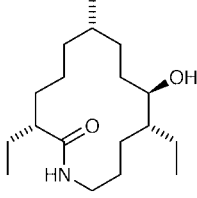


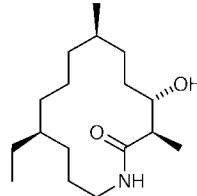
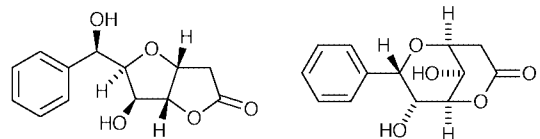
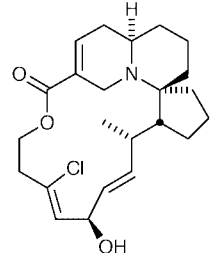
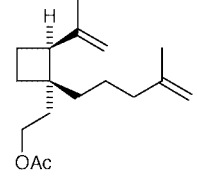
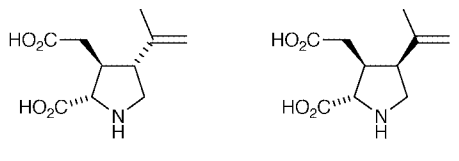
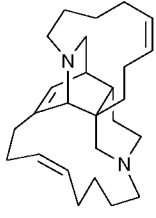
Robert Narquizian and Jacqueline Milne

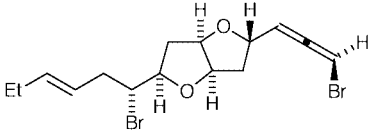
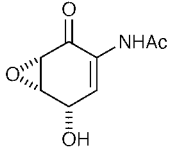
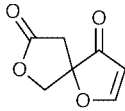
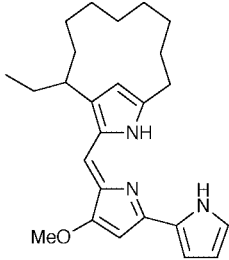
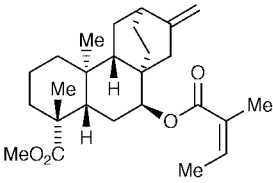
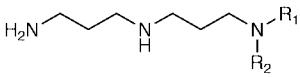
Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ

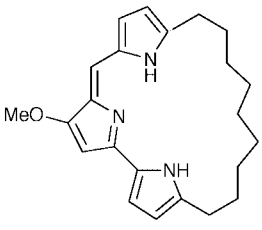
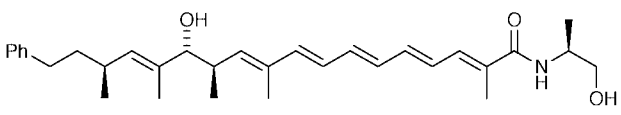
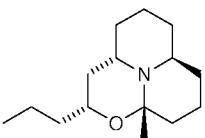
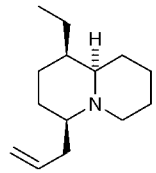
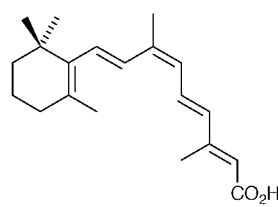
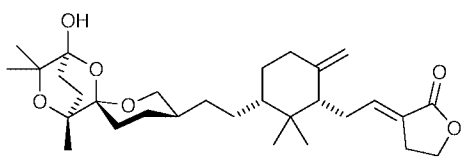
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

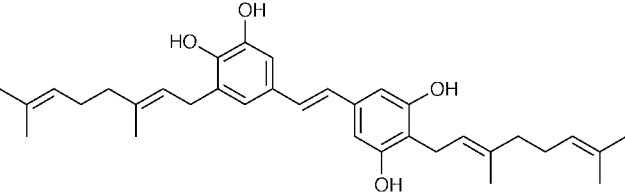
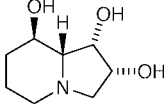
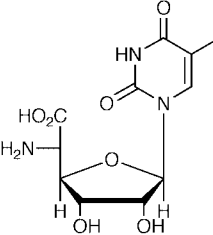
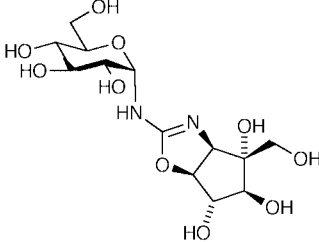
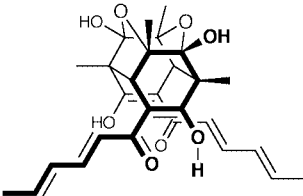
<p>Alboatrin</p> <p><i>Biological activity:</i> phytotoxic metabolite isolated from the culture filtrate of <i>Verticillium alboartrum</i>.</p> <p><i>Key steps:</i> radical-cyclisation mediated by 1-ethylpiperidine hypophosphite (1-EPHP).</p> <p>S. R. Graham, J. A. Murphy and A. R. Kennedy, <i>J. Chem. Soc., Perkin Trans. 1</i>, 1999, 3071.</p>	
<p>Avarol and Avarone</p> <p><i>Biological activity:</i> (a) antimitotic; (b) antileukemic; (c) antiviral.</p> <p><i>Key steps:</i> (a) L-phenylalanine-mediated asymmetric Robinson annulation to afford a Wieland-Miescher-type enone as starting material; (b) application of Barton's radical decarboxylation and quinone addition reaction to install the quinone nucleus.</p> <p>T. Ling, A. X. Xiang and E. A. Theodorakis, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3089.</p>	 <p style="text-align: center;">Avarol Avarone</p>
<p>(±)-Avenociolide, (+)-Dihydrocanadensolid and (±)-Isoavenociolide</p> <p><i>Biological activity:</i> (+)-Dihydrocanadensolid isolated as a mold metabolite of <i>Penicillium canadense</i>. Avenociolide and isoavenociolide are secondary metabolites isolated from <i>Aspergillus</i> and <i>Penicillium</i>.</p> <p><i>Key steps:</i> (a) intramolecular alkoxyacylation of propargyltungsten complexes to form tungsten-π,γ-lactonyl species; (b) condensation of CpW(NO)I(η-allyl) derivatives with aldehydes.</p> <p>M.-J. Chen, K. Narkunan and R.-S. Liu, <i>J. Org. Chem.</i>, 1999, 64, 8311.</p>	 <p style="text-align: center;">Avenociolide (+)-Dihydrocanadensolid Isoavenociolide</p>
<p>(±)-Bisorbibutenolide</p> <p><i>Biological activity:</i> antioxidant.</p> <p><i>Key steps:</i> biomimetic synthesis <i>via</i> a base-catalysed retro-Claisen reaction of bisorbicillinol.</p> <p>K. C. Nicolaou, K. B. Simonsen, G. Vassilikogiannakis, P. S. Baran, V. P. Vidali, E. N. Pitsinos and E. A. Couladouros, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3555.</p>	
<p>(±)-Bisorbicillinol</p> <p><i>Biological activity:</i> antioxidant.</p> <p><i>Key steps:</i> biomimetic synthesis involving Diels-Alder reaction of an oxidised form of sorbicillin.</p> <p>K. C. Nicolaou, K. B. Simonsen, G. Vassilikogiannakis, P. S. Baran, V. P. Vidali, E. N. Pitsinos and E. A. Couladouros, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3555.</p>	

<p>Coenzyme Q₃₋₈</p> <p><i>Biological activity:</i> implicated in electron-transfer processes necessary for respiration.</p> <p><i>Key steps:</i> fragment linkage via (a) sulfone-mediated alkylation followed by reductive cleavage; (b) Negishi Zr-mediated carboalumination; (c) Ni(0)-catalysed cross-coupling of an alkenylalane with a chloromethylated <i>p</i>-quinone</p> <p>B. H. Lipshutz, G. Bulow, F. Fernandez-Lazaro, S.-K. Kim, R. Lowe, P. Mollard and K. L. Stevens, <i>J. Am. Chem. Soc.</i>, 1999, 121, 11664.</p>	
<p>(±)-Cylindricines A and B</p> <p><i>Biological activity:</i> not reported.</p> <p><i>Key steps:</i> addition of an organocopper species to a bicyclic vinylogous amide.</p> <p>J. F. Liu and C. H. Heathcock, <i>J. Org. Chem.</i>, 1999, 64, 8263.</p>	 <p style="text-align: center;">Cylindricine A Cylindricine B</p>
<p>Cytochalasin D and O.</p> <p><i>Biological activity:</i> fungal metabolites which exhibit a wide range of biological activities including inhibition of cytoplasmic cleavage during cell division leading to the formation of multinuclear cells.</p> <p><i>Key steps:</i> intramolecular Diels–Alder reaction.</p> <p>E. Merifield and E. J. Thomas, <i>J. Chem. Soc., Perkin Trans. 1</i>, 1999, 3269.</p>	 <p style="text-align: center;">Cytochalasin D Cytochalasin O</p>
<p>Deoxyfrenolicin</p> <p><i>Biological activity:</i> belongs to the pyranonaphthoquinone family which exhibit significant biological activity against fungi, cancers and bacteria.</p> <p><i>Key steps:</i> DDQ-induced, oxidative C–C bond coupling reaction.</p> <p>Y.-C. Xu, D. T. Kohlman, S. X. Liang and C. Eriksson, <i>Org. Lett.</i>, 1999, 1, 1599.</p>	
<p>(+)-Discodermolide</p> <p><i>Biological activity:</i> (a) immunosuppressant; (b) antimitotic agent with similar activity to that of taxol; (c) promotes microtubule formation; (d) potent against multidrug resistant carcinoma cell lines.</p> <p><i>Key steps:</i> (a) three advanced intermediates derived from a common precursor; (b) modified Negishi coupling; (c) high pressure synthesis of a phosphonium salt; (d) Wittig linkage.</p> <p>A. B. Smith, M. D. Kaufman, T. J. Beauchamp, M. J. LaMarche and H. Arimoto, <i>Org. Lett.</i>, 1999, 1, 1823.</p>	
<p>Fluvirucinin B₁ (Sch 38516 aglycon)</p> <p><i>Biological activity:</i> (a) antifungal; (b) active against <i>Candida</i> sp. and dermatophytes; (c) active against influenza A virus.</p> <p><i>Key steps:</i> (a) diastereoselective acetate aldol reaction using the chiral boron derivative of Gennari <i>et al.</i>; (b) macrolactamisation from an (<i>S</i>)-2-pyridyl 13-azidothioester by reduction (with Sn(II)-PySH complexes) and cyclisation <i>in situ</i>.</p> <p>M. Martín, G. Mas, F. Urpí and J. Vilarrasa, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3087.</p>	

<p>Fluvirucine A₁</p> <p><i>Biological activity:</i> the title compound is the aglycon of fluvirucin A₁ which is an antiviral agent with low toxicity.</p> <p><i>Key steps:</i> (a) diastereoselective replacement of the carbonyl of 3-ethylvalerolactam with a vinyl group; (b) diastereoselective ring expansion of a 2-vinylpiperidine to a ten-membered lactam ring; (c) oxazolidinone-mediated aldol condensation.</p> <p>Y.-G. Suh, S.-A. Kim, J.-K. Jung, D.-Y. Shin, K.-H. Min, B.-A. Koo and H.-S. Kim, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3545.</p>	
<p>Goniofufurone and Goniopyrnone</p> <p><i>Biological activity:</i> antitumour activity.</p> <p><i>Key steps:</i> use of α-metallated 3-phenylsulfonyl orthopropionate as a homoenolate equivalent.</p> <p>J.-P. Surivet and J.-M. Vatable, <i>Tetrahedron</i>, 1999, 55, 13011.</p>	 <p style="text-align: center;">Goniofufurone Goniopyrnone</p>
<p>(+)-Halochlorine</p> <p><i>Biological activity:</i> the title compound, isolated from the marine sponge <i>Halichondria okadae</i>, inhibits induced expression of vascular cell adhesion molecule-1 (VCAM-1) which is implicated in inflammation disorders.</p> <p><i>Key steps:</i> (a) Pd-catalysed chain extension followed by intramolecular Michael reaction to generate the spirocyclic six-membered ring; (b) crossed Claisen reaction followed by an intramolecular Michael addition to generate the tetrahydropyridine ring; (c) hydrozirconation of a terminal alkyne.</p> <p>D. Trauner, J. B. Schwartz and S. J. Danishefsky, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3542.</p>	
<p>(1<i>R</i>,2<i>S</i>)-cis-2-Isopropenyl-1-(4'-methylpent-4'-en-1'-yl)-cyclobutylethyl acetate</p> <p><i>Biological activity:</i> sex pheromone of the oleander scale <i>Aspidiotus nerii</i>.</p> <p><i>Key steps:</i> (a) stereocontrolled and regioselective intramolecular <i>exo</i>-cyclisation of a <i>cis</i>-epoxynitrile to afford a cyclobutane alcohol; (b) Wittig reaction.</p> <p>I. Petschen, A. Parilla, M. P. Bosch, C. Amela, A. A. Botar, F. Camps and A. Guerrero, <i>Chem. Eur. J.</i>, 1999, 5, 3299.</p>	
<p>(+)-α-Allokainic Acid and (-)-α-Kainic Acid</p> <p><i>Biological activity:</i> neuroexcitatory amino acids.</p> <p><i>Key steps:</i> Ni-catalysed cyclisation of an alkyne onto an α,β-unsaturated carbonyl derivative was used to close the pyrrolidine ring.</p> <p>M. V. Chevliakov and J. Montgomery, <i>J. Am. Chem. Soc.</i>, 1999, 121, 11139.</p>	 <p style="text-align: center;">(+)-α-Allokainic Acid (-)-α-Kainic Acid</p>
<p>Keramaphidin B</p> <p><i>Biological activity:</i> isolated from <i>Amphimedon</i> sp. and <i>Xestospongia ingens</i>; biological activity not reported.</p> <p><i>Key steps:</i> Grubbs metathesis.</p> <p>J. E. Baldwin, T. D. W. Claridge, A. J. Culshaw, F. A. Heupel, V. Lee, D. R. Spring and R. C. Whitehead, <i>Chem. Eur. J.</i>, 1999, 5, 3154.</p>	

<p>(-)-Kumausallene</p> <p><i>Biological activity:</i> isolated from the red alga <i>Laurencia nipponica</i> Yamada; biological activity not reported.</p> <p><i>Key steps:</i> radical cyclisation of a vinylogous carbonate-acyl selenide using $(\text{TMS})_3\text{SiH}$ and Et_3B to form a cyclic ether.</p> <p>P. A. Evans, V. S. Murthy, J. D. Roseman and A. L. Rheingold, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3175.</p>	
<p>(-)-LL-C10037α</p> <p><i>Biological activity:</i> (a) antibacterial; (b) antitumour.</p> <p><i>Key steps:</i> (a) enzymatic resolution; (b) chemoselective azide reduction with a modified palladium on carbon; (c) tandem oxidation-β-elimination reaction.</p> <p>S. T. Murphy, J. R. Benesik and C. R. Johnson, <i>Org. Lett.</i>, 1999, 1, 1483.</p>	
<p>(±)-Longianone</p> <p><i>Biological activity:</i> isolated from the fungal strain <i>Xylaria longiana</i>; biological activity not reported.</p> <p><i>Key steps:</i> spirocyclic framework established by an intramolecular addition of a vinyl radical to a butenolide.</p> <p>P. G. Steel, <i>Chem. Commun.</i>, 1999, 2257.</p>	
<p>Metacycloprodigosin</p> <p><i>Biological activity:</i> immunosuppressive.</p> <p><i>Key steps:</i> (a) palladium-catalysed macrocyclisation reaction of a vinyl epoxide; (b) conversion of an α-pyrone derivative into a 2,4-disubstituted pyrrole ring; (c) Wittig olefination.</p> <p>A. Fürstner and H. Krause, <i>J. Org. Chem.</i>, 1999, 64, 8281.</p>	
<p>(±)-Methyl gummiferolate</p> <p><i>Biological activity:</i> the corresponding carboxylic acid shows plant growth-regulatory activity.</p> <p><i>Key steps:</i> (a) homoallyl-homoallyl radical rearrangement reaction to afford a highly functionalised bicyclo[2.2.2]octane from an enyne; (b) intramolecular Diels-Alder reaction of a tetraene.</p> <p>M. Toyota, M. Yokota and M. Ihara, <i>Org. Lett.</i>, 1999, 1, 1627.</p>	
<p>Motuporamines A-C</p> <p><i>Biological activity:</i> cytotoxic.</p> <p><i>Key steps:</i> ring-closure metathesis reaction.</p> <p>W. P. D. Goldring and L. Weiler, <i>Org. Lett.</i>, 1999, 1, 1471.</p>	 <p>Motuporamine A $\text{R}^1, \text{R}^2 = -(\text{CH}_2)_{12}-$ Motuporamine B $\text{R}^1, \text{R}^2 = -(\text{CH}_2)_{13}-$ Motuporamine C $\text{R}^1, \text{R}^2 = (Z) -(\text{CH}_2)_4-\text{CH}=\text{CH}-(\text{CH}_2)_8-$</p>

<p>Nonylprodigiosin</p> <p><i>Biological activity:</i> (a) deeply red pigment; (b) antibacterial; (c) cytotoxic; (d) antimalarial; (e) immunosuppressive activity at doses that are not cytotoxic.</p> <p><i>Key steps:</i> (a) palladium-catalysed Suzuki cross coupling; (b) ring closing metathesis reaction of a diene to form macrocyclic ring using a ruthenium indenylidene complex as precatalyst.</p> <p>A. Fürstner, J. Grabowski and C. W. Lehmann, <i>J. Org. Chem.</i>, 1999, 64, 8275.</p>	
<p>Phenalamide A₂</p> <p><i>Biological activity:</i> reverses multidrug resistance.</p> <p><i>Key steps:</i> (a) allylboration chemistry; (b) synthesis of a trienal by retro Diels–Alder reaction of 1,3-dioxine.</p> <p>R. W. Hoffmann, T. Rohde, E. Haerberlin and F. Schäfer, <i>Org. Lett.</i>, 1999, 1, 1713.</p>	
<p>(–)-Porantheridine</p> <p><i>Biological activity:</i> not reported.</p> <p><i>Key steps:</i> stereoselective nucleophilic substitution of the methoxy group of a bicyclic amino ether, <i>via</i> the corresponding <i>N</i>-acyl iminium ion.</p> <p>M. David, H. Dhimane, C. Vanucci-Bacqué and G. Lhommet, <i>J. Org. Chem.</i>, 1999, 64, 8402.</p>	
<p>(±)-Quinolizidine 2071</p> <p><i>Biological activity:</i> not reported.</p> <p><i>Key steps:</i> relative stereochemistry of 3 stereogenic centres established by constraints imposed by a 9-azabicyclo[3.3.1]nonane starting material.</p> <p>P. Michel and A. Rassat, <i>Chem. Commun.</i>, 1999, 2281.</p>	
<p>9-<i>cis</i>-Retinoic Acid</p> <p><i>Biological activity:</i> natural ligand of the retinoid X subfamily of nuclear receptors (RXRs), in particular RXR, a central regulator of hormone action.</p> <p><i>Key steps:</i> Suzuki reaction.</p> <p>Y. Pazos and A. R. de Lera, <i>Tetrahedron Lett.</i>, 1999, 40, 8287.</p>	
<p>(+)-Saponaceolide B</p> <p><i>Biological activity:</i> the saponaceolides A–D from the mushroom <i>Tricholoma saponaceum</i> possess antitumour activity against 60 human cancer cell lines.</p> <p><i>Key steps:</i> Pd-catalysed cycloisomerisation of an enyne.</p> <p>B. M. Trost and J. R. Corte, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3664.</p>	

<p>Schweinfurthin C</p> <p><i>Biological activity:</i> in contrast to Schweinfurthin A and B, the title compound lacks significant anticancer activity.</p> <p><i>Key steps:</i> Wittig reactions.</p> <p>E. M. Treadwell, S. C. Cermak and D. F. Wiemer, <i>J. Org. Chem.</i>, 1999, 64, 8718.</p>	
<p>(-)-Swainsonine</p> <p><i>Biological activity:</i> (a) potent inhibitor of both lysosomal α-mannosidase and mannosidase II; (b) has been selected for clinical testing as an anticancer drug.</p> <p><i>Key steps:</i> palladium-catalysed desymmetrisation of a <i>meso</i>-2-ene-1,4-diol.</p> <p>B. M. Trost and D. E. Patterson, <i>Chem. Eur. J.</i>, 1999, 5, 3279.</p>	
<p>Thymine polyoxin C</p> <p><i>Biological activity:</i> (a) nucleoside antibiotic; (b) agricultural fungicide.</p> <p><i>Key steps:</i> [3,3] sigmatropic rearrangement of an allylic trifluoroacetimidate to a trifluoroacetamide.</p> <p>A. Chen, E. J. Thomas and P. D. Wilson, <i>J. Chem. Soc., Perkin Trans. 1</i>, 1999, 3305.</p>	
<p>Trehazolin</p> <p><i>Biological activity:</i> inhibits trehalase which is implicated in insect metabolism and germination of ascospores of fungi.</p> <p><i>Key steps:</i> ketone-oxime ether reductive cyclisation promoted by SmI_2.</p> <p>I. S. de Gracia, S. Bobo, M. D. Martín-Ortega and J. L. Chiara, <i>Org. Lett.</i>, 1999, 1, 1705.</p>	
<p>(±)-Trichodimerol</p> <p><i>Biological activity:</i> inhibits tumour necrosis factor α (TNF-α); a lead compound for the treatment of septic shock.</p> <p><i>Key steps:</i> two-step Michael addition–ketalisation sequence involving an oxidised form of sorbicillin.</p> <p>K. C. Nicolaou, K. B. Simonsen, G. Vassilikogiannakis, P. S. Baran, V. P. Vidali, E. N. Pitsinos and E. A. Couladouros, <i>Angew. Chem., Int. Ed.</i>, 1999, 38, 3555.</p>	
<p>Xestobergsterol A</p> <p><i>Biological activity:</i> strong inhibitor of the release of histamines from mast cells.</p> <p><i>Key steps:</i> (a) Breslow remote functionalisation of a polyoxygenated steroid; (b) base-catalysed epimerisation-aldol condensation of a dione.</p> <p>M. E. Jung and T. W. Johnson, <i>Org. Lett.</i>, 1999, 1, 1671.</p>	