Total synthesis of cytochalasin D: total synthesis and full structural assignment of cytochalasin O

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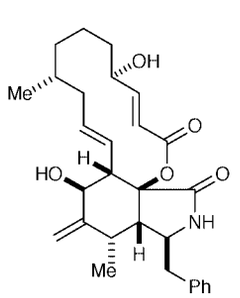
A total synthesis of cytochalasin D **3** is reported in which the key step is an intramolecular Diels–Alder reaction used to close the 11-membered ring simultaneously introducing the required stereochemistry at four of the stereogenic centres, C(4), C(5), C(8) and C(9). The precursor **21** for the Diels–Alder reaction was prepared from the aldehyde **13** by condensation with the dienyl phosphonate **14** to give the triene **15** which, after conversion into the acyl imidazole **17**, was used to acylate the pyrrolidinone **18**. The unstable pyrrolinone **21** was then generated from the pyrrolidinone by phenylselenation–oxidative elimination and was cyclised by heating in toluene under high dilution conditions to give the macrocyclic triene **22** (25–30%). Selective functionalisation of the double-bonds in this triene was investigated with epoxidation being selective for the 17,18-double-bond and hydroxylation using osmium tetroxide taking place selectively at the 6,7-double-bond. For completion of the synthesis of cytochalasin D **3**, the 6,7-diol **26** was converted into the exocyclic alkene **30** by protection and dehydration. Further hydroxylation using osmium tetroxide gave the diol **31** which was taken through to the enone **36** by protection followed by phenylselenation, *N*-debenzoylation and oxidative elimination. Reduction under Luche's conditions gave the alcohol **37** which was converted into the acetate **41** by acetylation followed by protecting group exchange. Selective deprotection of the vicinal diol and mild oxidation then gave the ketone **43**. Final deprotection gave cytochalasin D **3** so completing the first total synthesis of this natural product.

During the course of this work, the Diels–Alder adduct **22** was oxidised using an excess of osmium tetroxide to give the tetraol **28**. After protection as its bis-acetonide **46**, this was converted into the allylic acetate **51** using the chemistry developed during the synthesis of cytochalasin D **3**. Selective hydrolysis of the 17,18-acetonide and oxidation under Swern conditions gave the hydroxyketone **53** which on deprotection gave cytochalasin O **54** so confirming the structure of this natural product.

The cytochalasans together with the chaetoglobosins and aspochalasans constitute a group of 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.[1,2] Structurally they are characterised by the presence of a hydrogenated isoindolone unit fused to a macrocyclic ring which can either be a lactone, a carbonate or a carbocycle as exemplified by cytochalasins B **1**,[2] E **2**[3] and D **3**,[2] respectively.

The total synthesis of cytochalasans has been of considerable interest for several years[4] and both inter- and intramolecular Diels–Alder reactions have been used to assemble the isoindolone components stereoselectively.[4–6] In addition, elegant ring-expansion[7] and fragmentation[8] procedures have been developed to generate the eleven-membered ring of the [11]cytochalasans which has also been formed using a Reformatski reaction.[9] A total synthesis of a structurally related aspochalasan, aspochalasin C, has also been reported in which a palladium(0) catalysed macrocyclisation was a key step.[10]

We have been interested in developing total syntheses of [11] and [13]cytochalasans using an intramolecular Diels–Alder reaction to close the 11- or 13-membered ring with simultaneous stereoselective formation of the reduced isoindolone component.[4] This strategy has been used to complete total syntheses of cytochalasin H **4**,[11] proxiphomin **5**,[12] cytochalasin G **6**[13] and the (13*Z*)-iso-aspochalasin **7**.[14] We now report full details of a total synthesis using this approach of cytochalasin D **3**, one of the first fully functionalised cytochalasans to be characterised and one which has potent biological activity. During the course of our work, a new cytochalasin, cytochalasin O,[15] was also synthesized to establish unambigously its stereochemistry at C(5) and C(6).



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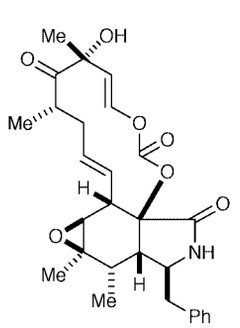

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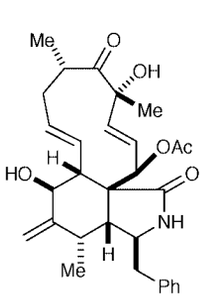

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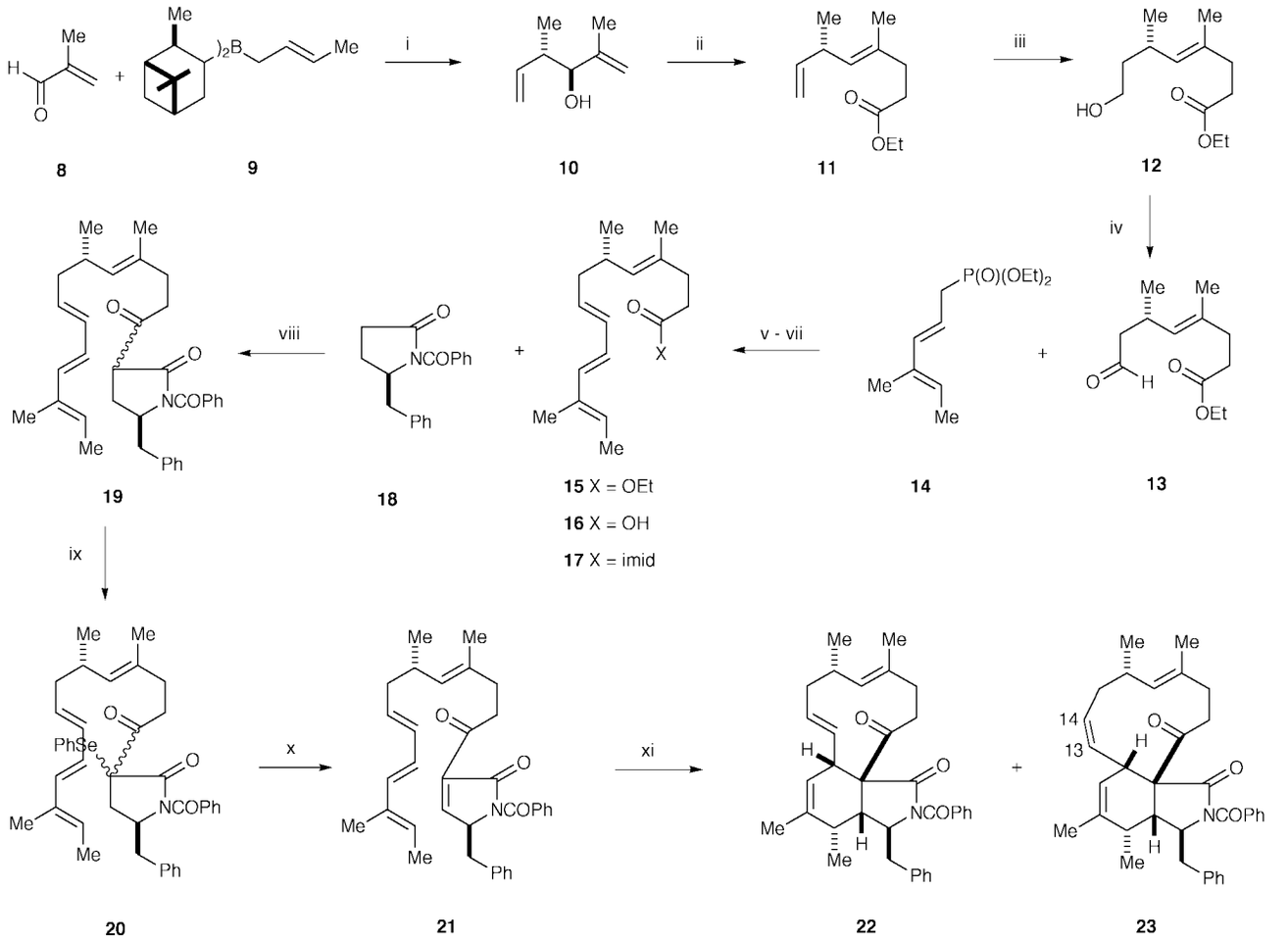
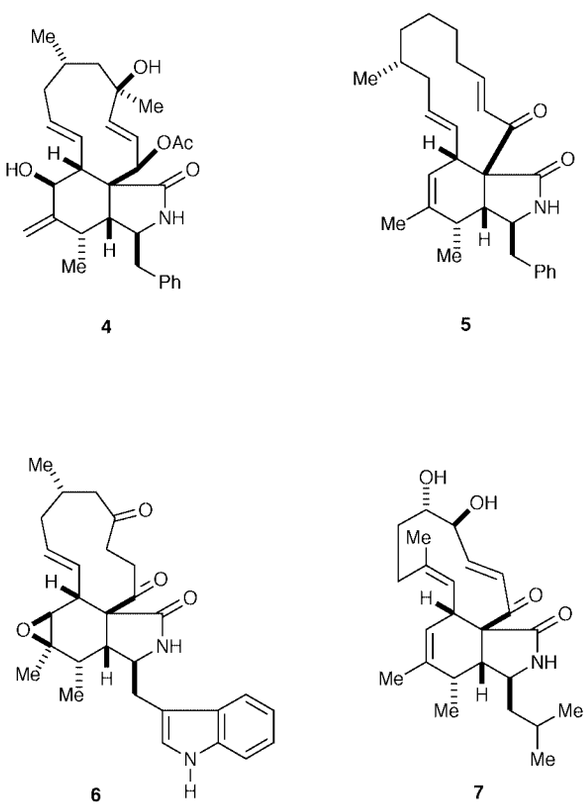
Different variations of the intramolecular Diels–Alder strategy can be envisaged for the synthesis of cytochalasans.[4] The chiral centres around the macrocyclic ring can be introduced either before or after the Diels–Alder reaction. In the



Scheme 1 *Reagents and conditions:* i, −78 °C, 3 h, then H_2O_2; ii, $MeC(OEt)_3$, propanoic acid, 140–170 °C (48% from **8**); iii, 9-BBN then H_2O_2 (77%); iv, $(COCl)_2$, dimethyl sulfoxide (77%); v, *n*-BuLi, **14**, tetrahydrofuran, hexamethylphosphoramide (85%); vi, NaOH, ethanol; vii, $CO(imidazole)_2$, tetrahydrofuran; viii, $LiN(SiMe_3)_2$, **18** (92% from **15**); ix, $LiN(SiMe_3)_2$, PhSeCl (100%); x, *m*-chloroperoxybenzoic acid, H_2O_2, −50 °C to 0 °C; xi, toluene, 80 °C (25–30% from **20**).

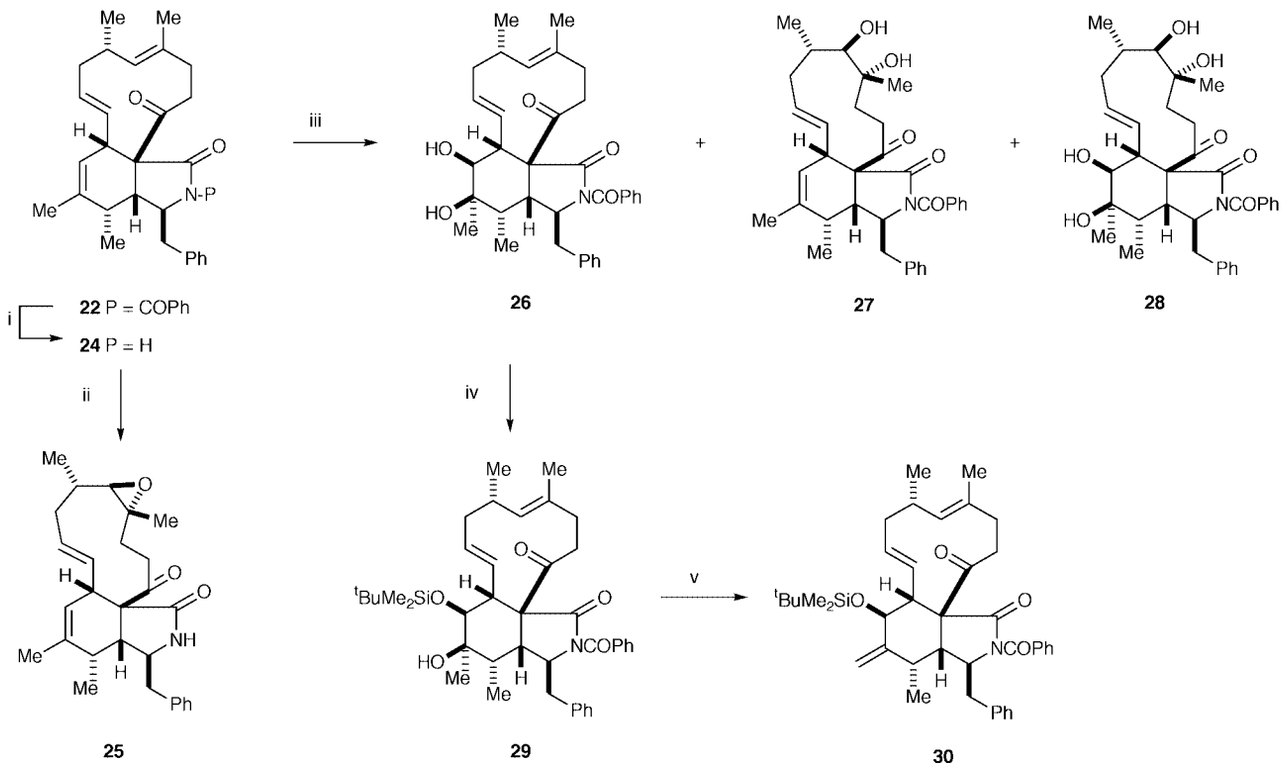


present synthesis of cytochalasin D **3**, only the chiral centres at C(16) and C(3) are present before the cyclisation. The rest are introduced either during the Diels–Alder reaction itself or later in the synthesis using the conformational preference of the macrocyclic ring to control stereochemistry.[16]

Results and discussion

Total synthesis of cytochalasin D

The synthesis of the pyrrolinone **21** and its cyclisation leading to the cytochalasan **22** are outlined in Scheme 1. The reaction between methacrolein **8** and (*E*)-but-2-enyldiisopinocampheylborane **9**, prepared from (+)-pinene, gave the *anti*-homoallylic alcohol **10** after oxidative work-up, together with about 10% of its *syn*-diastereoisomer.[17] The major *anti*-alcohol was estimated to have an ee of 84% from its Mosher's derivatives although the minor *syn*-alcohol appeared to be racemic. This mixture of *anti*- and *syn*-alcohols was not separated; instead it was heated with triethyl orthoacetate, a catalytic amount of propionic acid and hydroquinone (as a radical scavenger) to effect a Claisen rearrangement[18] to give the (*E*)-ester **11** which was isolated in an overall yield of 48% from methacrolein. The (*E*)-geometry of the trisubstituted double-bond in **11** was assigned on the basis of precedent[19] and was confirmed later on in the synthesis. Regioselective monohydroboration of diene **11** using 9-borabicyclononane with an oxidative work-up gave the alcohol **12** in a yield of 75% after distillation, the side-product, cyclooctane-1,5-diol, being removed by crystallisation. The optical purity of this alcohol



Scheme 2 *Reagents and conditions:* i, sodium hydroxide, aq. methanol (95%); ii, *m*-chloroperoxybenzoic acid, −25 °C (92%); iii, osmium tetroxide, pyridine (**26**, 53%; **27**, 4%; **28**, 16%); iv, *tert*-butyldimethylsilyl triflate, 2,6-lutidine (89%); v, thionyl chloride, triethylamine (85%).

was found to correspond to an ee of *ca*. 75% (Mosher's derivatives). The (*S*)-configuration was initially assigned on the basis that (+)-pinene had been used to prepare the crotylborane **9**. To check this assignment, the alcohol was ozonolysed with reduction of the ozonide using sodium borohydride. This procedure gave the laevorotatory 2-methylbutane-1,4-diol which is known to correspond to the (*S*)-enantiomer.[20]

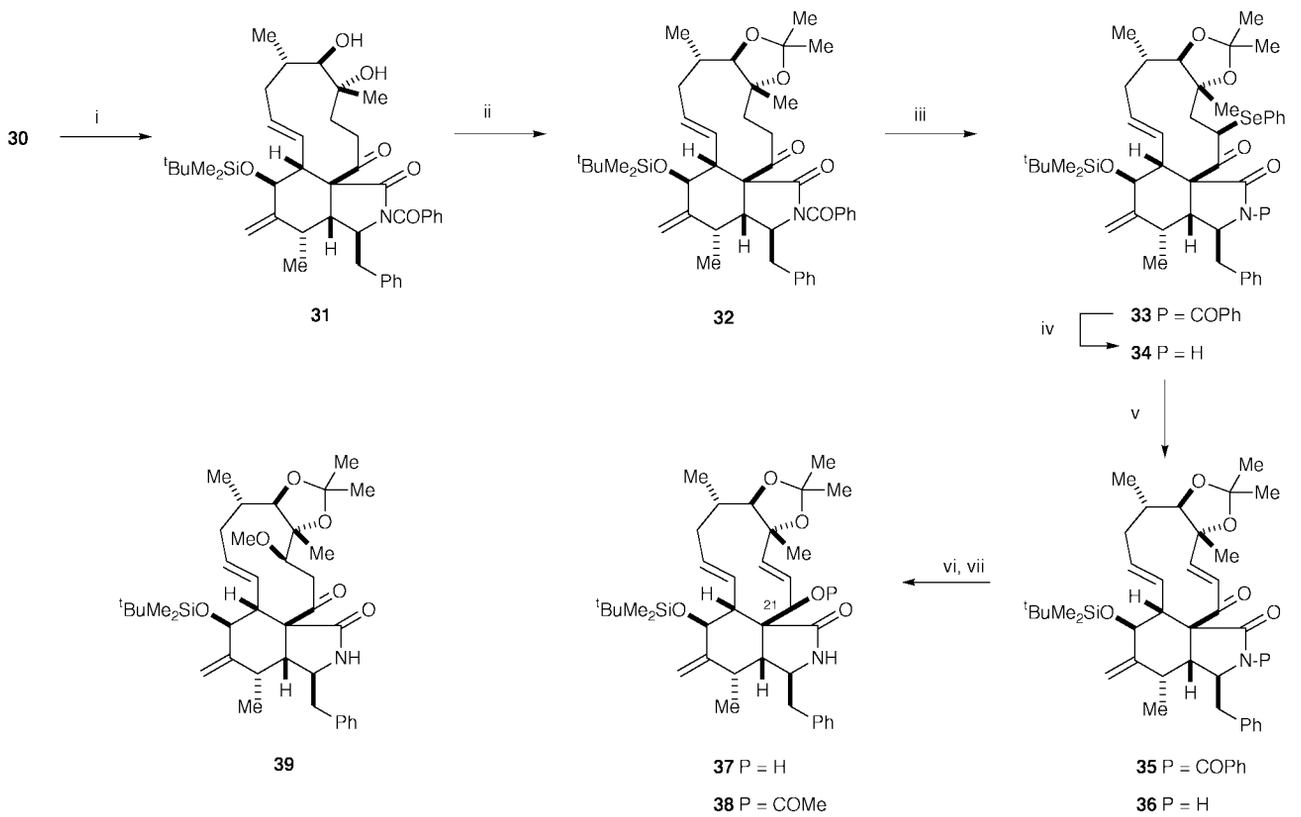
Oxidation of the alcohol **12** under Swern conditions gave the aldehyde **13** which was condensed with the dienyl phosphonate **14**[6] to give the (*E*,*E*,*E*)-conjugated triene **15** containing about 10% of its (*Z*,*E*,*E*)-isomer, in a combined yield of about 85%. The conditions for this condensation had been optimized previously[4] and the expected (*E*,*E*,*E*)-geometry of the major product was confirmed by ^{1}H NMR. Hydrolysis of the ester **15** gave the acid **16** which was converted into the acyl imidazole **17** by treatment with carbonyldiimidazole. This amide was used to acylate the *N*-benzoylpyrrolidinone **18**[21] to give the 3-acylpyrrolidinone **19** as a mixture of epimers and the pyrrolidinone was converted into the unstable 3-acylpyrrol-2(5*H*)-one **21** by phenylselenenylation followed by oxidative elimination. No attempt was made to isolate the pyrrolinone **21**; rather a solution of the crude product was diluted with toluene and heated at 80 °C to effect the Diels–Alder cyclisation. The major product from this reaction was identified as the required adduct **22** which was isolated in a yield of *ca*. 30% based on the pyrrolidinone **19**. A second, minor, adduct was also isolated in a yield of *ca*. 4% and was identified as the (13*Z*)-isomer **23**.

The adducts **22** and **23** were initially identified as *endo*-products formed by approach of the diene onto the less hindered face of the dienophile on the basis of precedent[4] and their structures were confirmed by extensive ^{1}H NMR studies. For example, for both isomers, significant NOE enhancements of H(3) were observed on irradiation of the 6-Me, consistent with the *endo*-stereochemistry shown. The structure of the major adduct **22** was also confirmed by its conversion into cytochalasin D **3**. For the minor adduct **23**, a substantial enhancement of H(14) was observed on irradiation of H(13) pointing to the presence of a (*Z*)-13,14-double-bond. This adduct would appear to have been formed by cyclisation of the minor (*Z*,*E*,*E*)-conjugated triene in the Diels–Alder precursor.

This 11-step synthesis from methacrolein made the [11]cytochalasin **22** available for further studies. It was now intended to use conformational control to introduce the remaining chiral centres, but in order to do this it was necessary to find chemistry which would discriminate between the different double-bonds.

N-Debenzoylation of the Diels–Alder adduct **22** gave the *NH*-lactam **24** which on epoxidation gave the 17,18-epoxide **25** highly regio- and stereo-selectively, see Scheme 2. The configuration of the epoxide was established as shown by NOE studies and is consistent with epoxidation taking place on the more exposed face of the alkene. Preliminary attempts to react the epoxide with nucleophiles were unsuccessful, probably because S_N2 ring-opening is severely hindered by the macrocyclic ring and so the chemistry of this epoxide was not studied any further. In contrast to the epoxidation, oxidation of the Diels–Alder adduct **22** using osmium tetroxide was selective for the 6,7-double-bond giving the diol **26** as the major product (53%) although small amounts of the isomeric diol **27** (4%) and the tetrol **28** (16%) were also obtained together with some recovered starting material (20%). Selective mono-protection of the secondary hydroxy group of the major diol using *tert*-butyldimethylsilyl triflate gave the silyl ether **29** which was dehydrated using thionyl chloride and triethylamine to give the exocyclic alkene **30** so completing the required functionalisation of the 6-membered ring.

The next stages involved selective functionalisation of the macrocycle, see Scheme 3. Oxidation of the triene **30** using osmium tetroxide was regioselective in favour of the trisubstituted alkene and gave the 17,18-diol **31** *via* attack on the less hindered face of the double-bond. After protection of the diol as its acetonide **32**, phenylselenenylation at C(20) was carried out using lithium diisopropylamide and benzeneselenenyl chloride. The selenide **33** was isolated as a single diastereoisomer, the configuration at C(20) being assigned on the basis of NOE studies. Oxidative elimination then gave the enone **35** but attempts to reduce this ketone to the corresponding alcohol

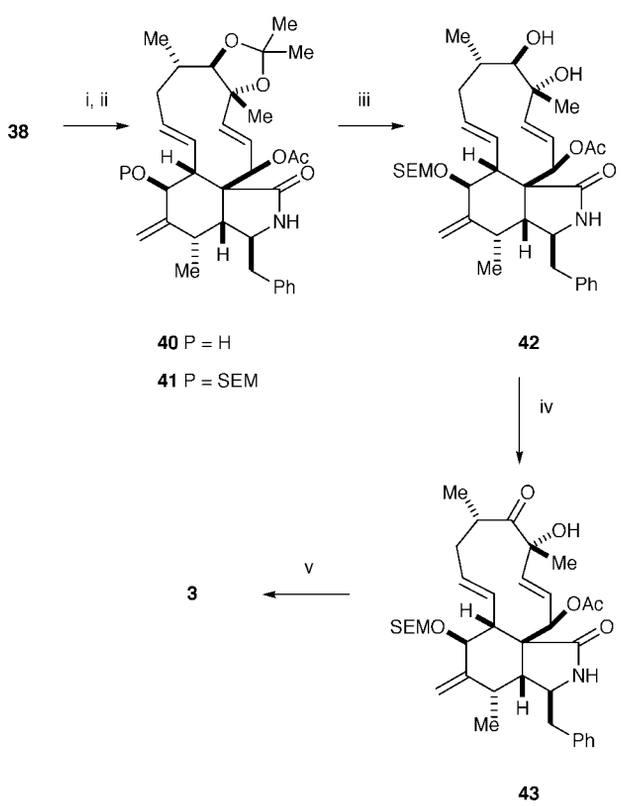


Scheme 3 *Reagents and conditions:* i, osmium tetroxide, pyridine (75%); ii, 2,2-dimethoxypropane, toluene-*p*-sulfonic acid (cat.) (99%); iii, lithium diisopropylamide, benzeneselenenyl chloride, −35 °C (70%); iv, sodium hydroxide, aqueous methanol (97%); v, aqueous hydrogen peroxide, pyridine (**35**, 67%; **36**, 65%); vi, sodium borohydride, cerium(III) chloride (93%); vii, acetic anhydride, triethylamine, DMAP (81%).

were accompanied by competing *N*-debenzoylation. Moreover, removal of the *N*-benzoyl group from the enone **35** using sodium hydroxide in aqueous ethanol was complicated by conjugate addition of the methanol to give the 19-methoxy derivative **39**.

To avoid these side reactions, the *N*-debenzoylation was carried out at the selenide stage to give the *NH*-lactam **34** which on oxidative elimination gave the enone **36**. Reduction under Luche's conditions[22] gave a good yield of the alcohol **37** which was converted into its acetate **38**. The configurations of the alcohol **37** and acetate **38** at C(21) were not established at this stage, but were confirmed later by the successful synthesis of cytochalasin D **3**.

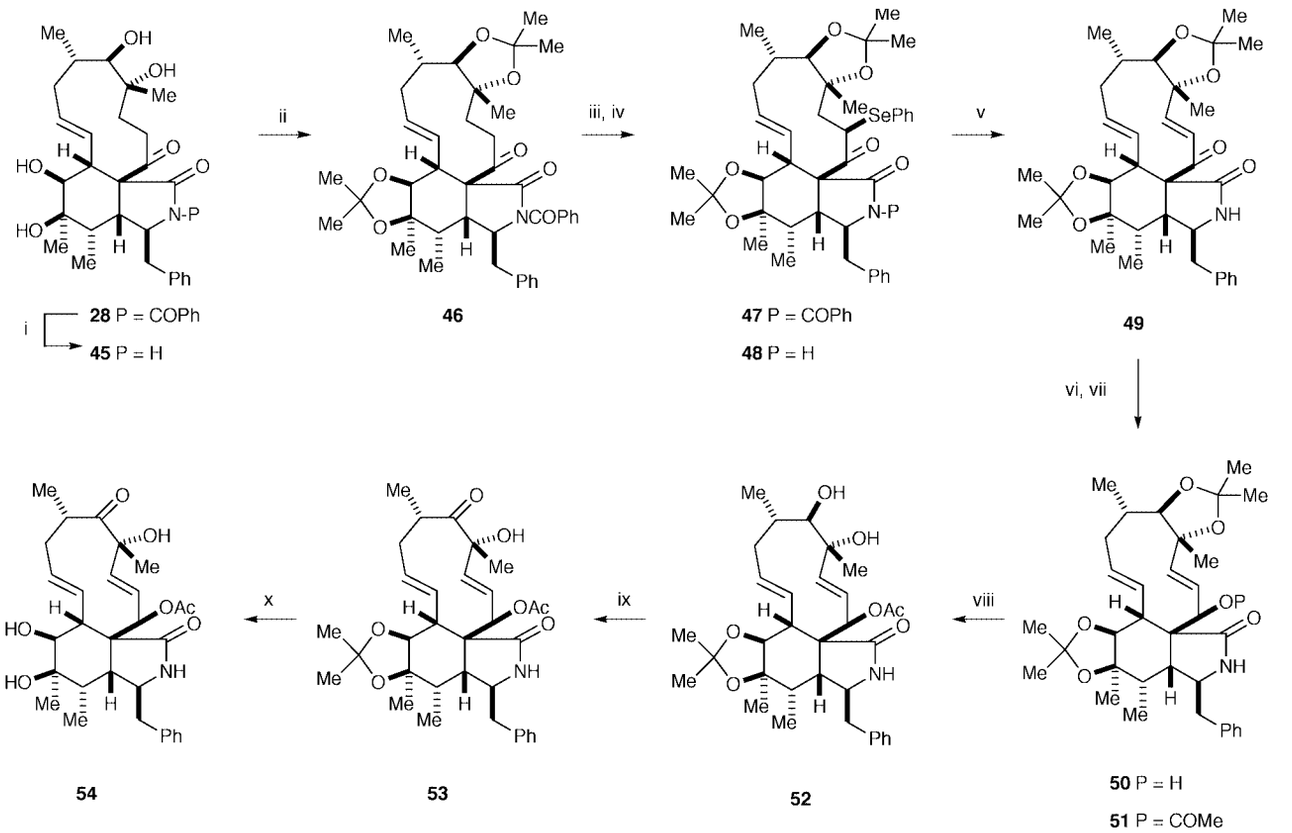
As preliminary attempts to hydrolyse the acetonide group of **38** were accompanied by loss of the *tert*-butyldimethylsilyl group, it was necessary to exchange this for a more acid stable protecting group before the oxidation of the 17-alcohol could be attempted, see Scheme 4. This was achieved by treatment of the silyl ether **38** with tetrabutylammonium fluoride followed by conversion of the alcohol **40** into its 2-trimethylsilylethoxymethyl (SEM) ether **41**. Acid catalysed hydrolysis then gave the 17,18-diol **42** which was oxidised under Swern conditions to the ketone **43**. Finally, deprotection of the 7-hydroxy group gave cytochalasin D **3** which was identical to an authentic sample of the natural product by IR, NMR, MS, $[\alpha]_D$, TLC, with data corresponding to those in the literature,[23] so completing the first total synthesis of this complex natural product.



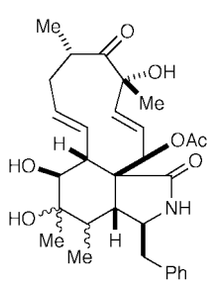
Scheme 4 *Reagents and conditions:* i, tetrabutylammonium fluoride, tetrahydrofuran (72%); ii, SEMCl, Hunig's base (74%); iii, aqueous HCl, tetrahydrofuran (64%); iv, oxalyl chloride, dimethyl sulfoxide, triethylamine (75%); v, HF, aq. acetonitrile (69%).

Total synthesis of cytochalasin O

During the course of this work, the structures of several new cytochalasans were published including that of cytochalasin O.[15] This was identified as the [11]cytochalasan **44** although the



Scheme 5 *Reagents and conditions*: i, sodium hydroxide, aq, methanol (73%); ii, 2,2-dimethoxypropane, toluene-*p*-sulfonic acid; iii, lithium diisopropylamide, benzeneselenenyl chloride (52% from **28**); iv, sodium hydroxide, aq. methanol; v, aq. hydrogen peroxide, pyridine (88% from **47**); vi, sodium borohydride, cerium(III) chloride (96%); vii, acetic anhydride, triethylamine, DMAP (81%); viii, toluene-*p*-sulfonic acid in methanol (74%); ix, oxalyl chloride, dimethyl sulfoxide, triethylamine (66%); x, aq. hydrogen chloride, methanol, heat under reflux (78%).



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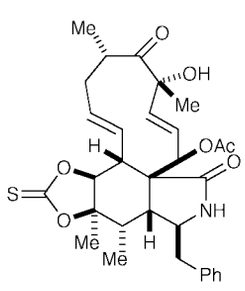
configurations of the chiral centres at C(5) and C(6) were not assigned. Whilst investigating alternative routes from the Diels–Alder adduct **22** to cytochalasin D **3**, a synthesis of cytochalasin O was developed which enabled its full structure to be established.

Oxidation of the Diels–Alder adduct **22** with an excess of osmium tetroxide gave the tetraol **28** as the major product (69%). This was converted into the bis-acetonide **46** using 2,2-dimethoxypropane under acidic conditions, (see Scheme 5) and the bis-acetonide taken through the sequence previously developed of phenylselenation, *N*-deprotection, oxidative elimination, ketone reduction and *O*-acetylation to give the allylic acetate **51**. Selective hydrolysis of the 17,18-acetonide was then accomplished using toluene-*p*-sulfonic acid in ethanol and the diol **52** so obtained oxidised under Swern conditions to give the ketone **53**. Hydrolysis of the remaining acetonide was then carried out using dilute aqueous hydrogen chloride in methanol and gave the 6,7-diol **54** which was found to have spectroscopic and physical properties identical to those of cytochalasin O[15] so establishing the full structure for cytochalasin O as indicated in structure **54**. In particular, a significant enhancement of the peak due to H(3) was observed in its ^{1}H NMR spectrum on irradiation of the 6-Me group consistent with the stereochemistry depicted for C(6).

To check that no epimerisation had taken place at C(6) during the final acetonide hydrolysis, the bis-acetonide **46** was subjected to the same conditions, *i.e.* hydrolysis in acidic methanol heated under reflux. This resulted in hydrolysis of both of the acetonide groups and removal of the *N*-benzoyl group to give the fully deprotected tetraol **45** which was identical to a sample prepared by *N*-debenzoylation of the tetrol **28** under basic conditions so confirming that epimerisation at C(6) had not occurred under the acidic hydrolysis conditions. Finally, cytochalasin O **54** was converted into its cyclic thiocarbonate **55** as a final check that the hydroxy groups at C(6) and C(7) were *cis*-disposed about the six-membered ring.



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Conclusions

This work has resulted in the completion of the first total synthesis of cytochalasin D **3** and a synthesis of cytochalasin O **54** which has enabled its structure to be fully assigned. The completion of these syntheses illustrates the usefulness of the intramolecular Diels–Alder strategy for the total synthesis of

complex natural products and provides examples of how conformational control can be used to introduce chiral centres stereoselectively into macrocyclic rings.

Experimental †

IR spectra were recorded on Perkin-Elmer 297, 257, or 1710 spectrometers as thin films unless otherwise specified. ^{1}H NMR spectra were recorded on Bruker AM 500, Bruker WH 300 and AC 300 spectrometers in $CDCl_3$ unless otherwise stated. Optical rotations were measured on Perkin-Elmer 241 and Optical Activity AA-100 polarimeters. Mass spectra were recorded on VG-Micromass 16F, VG-Micromass ZAB-16F, Kratos Concept and Varian Micromass 7070 spectrometers using electron impact (EI), chemical ionisation (CI) and fast atom bombardment (FAB) techniques. Characteristic groups of isotope peaks were obtained for compounds containing selenium; the peaks corresponding to ^{80}Se are quoted. Chromatography refers to flash chromatography using Merck silica gel 60 (230–400 mesh) or May and Baker Sorbsil C60 (40–60 mm). Base washed silica was prepared by washing flash silica with saturated aqueous potassium hydrogen carbonate then with distilled water until the washings were neutral, followed by drying at 100 °C for 3 days. HPLC was performed on a Dynamax Macro-HPLC column using a Gilson model 303 pump and model 131 refractive index detector.

Solvents and commercially available reagents were dried and purified by standard procedures. Ether refers to diethyl ether, THF to tetrahydrofuran and light petroleum to the fraction boiling in the range 40–60 °C. All air and moisture sensitive reactions were carried out under an atmosphere of dry nitrogen or argon.

(3*S*,4*S*)-2,4-Dimethylhexa-1,5-dien-3-ol 10

(+)-α-Pinene (69 cm^3, 434 mmol) was added to a solution of borane–dimethyl sulfide complex (22 cm^3, 220 mmol) in THF (65 cm^3). After 3 h at this temperature, dimethyl sulfide and THF were removed under reduced pressure (0.1 mmHg, 0 °C for 3 h). Further THF (80 cm^3) and (+)-α-pinene (10.5 cm^3, 66 mmol) were added and the mixture stored at 0 °C for 4 days. Methanol (17.5 cm^3, 432 mmol) was carefully added dropwise at 0 °C and, after a further 1 h at this temperature, concentration under reduced presssure (0.1 mmHg, 20 °C) gave methoxydi-(+)-isopinocampheylborane as a thick, colourless oil.

(*E*)-But-2-ene (35 cm^3, 377 mmol) was added to a mechanically stirred solution of potassium *tert*-butoxide (22.2 g, 198 mmol) in THF (150 cm^3) at −70 °C followed by a pre-cooled solution of butyllithium (198 mmol) in THF (80 cm^3). The resulting orange solution was allowed to warm to −45 °C, stirred for 10 min, then re-cooled to −70 °C. The methoxydi-(+)-isopinocampheylborane was dissolved in ether (150 cm^3), cooled to −70 °C and transferred to the crotylpotassium *via* cannula. After 30 min at −70 °C, boron trifluoride–diethyl ether (30.5 cm^3, 248 mmol) was added followed by a solution of methacrolein (21.6 cm^3, 261 mmol) in ether (50 cm^3) with vigorous stirring. After 3 h at −70 °C the mixture was treated with aqueous sodium hydroxide (3 M; 138 cm^3, 414 mmol) and aqueous hydrogen peroxide (30%; 66 cm^3, 582 mmol) then heated under reflux for 1 h. The mixture was filtered through Celite, the organic phase washed with water (200 cm^3), brine (150 cm^3) and the aqueous layers re-extracted with ether (2 × 150 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was fractionally distilled through a short Vigreux column and material boiling in the range 40–100 °C, 20 mmHg collected (20.5 g). Subsequent chromatography of a small amount using ether–light petroleum (1:12) as eluant provided a sample of the *title compound* **10** as a colourless oil containng *ca.* 10% of its *syn*-diastereoisomer (Found: M$^+$, 126.1040. $C_8H_{14}O$ requires *M*, 126.1045); $[\alpha]_D^{20}$ −29 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} 3400, 3075, 1640, 1450, 1370, 1220, 1110, 1010 and 900; δ_H (major isomer) 0.98 (3 H, d, *J* 7.5, 4-Me), 1.75 (3 H, s, 2-Me), 1.82 (1 H, s, exch. D_2O, OH), 2.33 (1 H, m, 4-H), 3.76 (1 H, d, *J* 11, 3-H), 4.92 and 5.16 (each 2 H, m, vinylic H) and 5.78 (1 H, m, 5-H); δ_H (minor isomer) 1.02 (3 H, d, *J* 7, 4-Me) and 3.9 (1 H, d, *J* 5, 3-H); *m*/*z* (CI) 144 (M$^+$ + 18, 17%), 127 (M$^+$ + 1, 38), 126 (M$^+$, 100) and 109 (M$^+$ − 17, 95).

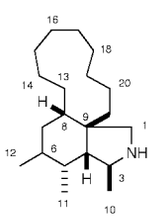
Ethyl (4*E*,6*S*)-4,6-dimethylocta-4,7-dienoate 11

A mixture of the *anti*-alcohol **10** and its *syn*-isomer prepared as above (*ca.* 9:1; 17.5 g, 139 mmol), triethyl orthoacetate (110 cm^3), propionic acid (0.5 cm^3, 6.7 mmol) and hydroquinone (0.5 g, 4.5 mmol) was heated to 140 °C with loss of ethanol through a short Vigreux column. The temperature was gradually increased to 170 °C until ethanol no longer distilled over. The excess of triethyl orthoacetate (bp 45 °C, 20 mmHg) was removed by distillation and the residue fractionally distilled to provide the *title compound* **11** (18.5 g, 48% from methacrolein) as a colourless oil, bp 80–82 °C, 0.5 mmHg (Found: M$^+$, 196.1460. $C_{12}H_{20}O_2$ requires *M*, 196.1463); $[\alpha]_D^{20}$ −12 (*c* 1.3 in $CHCl_3$); ν_{max}/cm^{-1} 3080, 1740, 1450, 1370, 1160 and 910; δ_H 1.05 (3 H, d, *J* 8, 6-Me), 1.28 (3 H, t, *J* 9, OCH_2CH_3), 1.63 (3 H, d, *J* 2, 4-Me), 2.25–2.5 (4 H, m, 2-H_2, 3-H_2), 3.07 (1 H, m, 6-H), 4.13 (2 H, q, *J* 9, OCH_2CH_3), 4.87–5.05 (3 H, m, 8-H_2, 5-H) and 5.77 (1 H, ddd, *J* 18, 11, 5, 7-H); *m*/*z* (CI) 214 (M$^+$ + 18, 5%) and 197 (M$^+$ + 1, 100).

Ethyl (4*E*,6*S*)-8-hydroxy-4,6-dimethyloct-4-enoate 12

A solution of 9-borabicyclononane in THF (0.5 M; 203 cm^3, 102 mmol) was added to the diene **11** (16.7 g, 85 mmol). After 3 h at room temperature, the solution was cooled to 5 °C then water (100 cm^3), aqueous sodium hydroxide (3 M; 150 cm^3) and aqueous hydrogen peroxide (30%; 160 cm^3) were added successively with careful maintenance of the temperature at between 5 and 10 °C (external bath temperature −40 to −70 °C). After the addition, the mixture was warmed to room temperature and stirred for 1 h then extracted with dichloromethane (2 × 250 cm^3) and the extracts washed with brine (120 cm^3), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was dissolved in ether–light petroleum (1:1; 40 cm^3) and stored at −30 °C for 48 h. The solid cyclooctane-1,5-diol was filtered off, washed with ether–light petroleum and the filtrate concentrated under reduced pressure. Distillation of the residue gave the *title compound* **12** (14 g, 77%) as a colourless oil, bp 118–122 °C, 1.5 mmHg (Found: M$^+$, 214.1561. $C_{12}H_{22}O_3$ requires *M*, 214.1569); $[\alpha]_D^{20}$ +23 (*c* 1.3 in $CHCl_3$); ν_{max}/cm^{-1} 3400, 3040, 1735, 1450, 1370, 1340, 1160 and 1050; δ_H 0.95 (3 H, d, *J* 7.5, 6-Me), 1.27 (3 H, t, *J* 7.5, OCH_2CH_3), 1.39 (1 H, br s, exch. D_2O, OH), 1.45 (2 H, m, 7-H_2), 1.63 (3 H, d, *J* 2, 4-Me), 2.25–2.45 (4 H, m, 2-H_2, 3-H_2),

† In this discussion, the nomenclature devised for the cytochalasans is used for compounds **22** onwards (ref. 24). Formula **i** shows the structure and numbering of the [11]cytochalasan nucleus. Additional structural features are indicated by conventional prefixes and suffixes.



i

2.52 (1 H, m, 6-H), 3.6 (2 H, m, 8-H_2), 4.12 (2 H, q, *J* 7.5, OCH_2CH$_3$) and 4.97 (1 H, d, *J* 10, 5-H); *m/z* (CI) 232 (M^+ + 18, 2%), 215 (M^+ + 1, 100), 169 (40) and 137 (16).

A mixture of alcohol **12** (24 mg, 111 mmol), pyridine (0.15 cm^3, 1.9 mmol) and (*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (0.04 cm^3, 0.23 mmol) in dichloromethane (1 cm^3) was stirred at room temperature for 24 h. The reaction was quenched with water (2 cm^3), extracted with dichloromethane (2 × 10 cm^3) and the organic layers dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–light petroleum (1:20) as eluant gave the (*S*)-Mosher's derivative (37 mg, 77%); ν_{max}/cm^{-1} 3060, 1740, 1450, 1370, 1340, 1260, 1160, 1120, 1080, 1025, 850, 760, 715 and 690; δ_H 0.95 (3 H, d, *J* 7.5, 6-Me), 1.28 (3 H, t, *J* 7.5, OCH$_2$CH_3), 1.55 (3 H, s, 4-Me), 1.72 (2 H, m, 7-H_2), 2.27–2.51 (5 H, m, 2-H_2, 3-H_2, 6-H), 3.58 (3 H, s, OMe), 4.2 (3 H, m, 8-H, OCH_2CH$_3$), 4.35 (1 H, m, 8-H), 4.93 (1 H, d, *J* 11, 5-H) and 7.42–7.60 (5 H, m, ArH); δ_F −73.5, −73.41 (ratio 87:13); *m/z* (CI) 448 (M^+ + 18, 10%), 431 (M^+ + 1, 78) and 196 (100).

The ester **12** (828 mg, 3.9 mmol) in ethanol (5 cm^3) was ozonolysed for 2.5 h at −78 °C. The solution was then degassed with oxygen, warmed to 0 °C and transferred to a mixture of sodium borohydride (306 mg, 8.1 mmol) and sodium hydroxide (288 mg, 7.2 mmol) in ethanol–water (1:1) (6 cm^3) at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight after which the product was extracted with ethyl acetate (3 × 25 cm^3) and the organic extracts dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–light petroleum (5:1) as the eluant gave (*S*)-2-methylbutane-1,4-diol (301 mg, 75%) as a colourless oil; $[\alpha]_D^{20}$ −10 (*c* 0.7 in MeOH) [lit.,[20] −13.4 (*c* 0.7 in MeOH)]; ν_{max}/cm^{-1} 3350, 1660, 1457, 1381, 1060, 1039 and 1006; δ_H 0.95 (3 H, d, *J* 8, 2-Me), 1.59 (2 H, m, 3-H_2), 1.82 (1 H, m, 2-H), 2.90 (2 H, br s, 2 × OH), 3.44 (1 H, dd, *J* 9.5, 7.5, 1-H), 3.57 (1 H, dd, *J* 9.5, 6, 1-H) and 3.68 and 3.77 (each 1 H, m, 4-H); *m/z* (CI) 122 (M^+ + 18, 36%) and 105 (M^+ + 1, 100).

Ethyl (4*E*,6*S*)-7-formyl-4,6-dimethylhept-4-enoate 13

To a solution of oxalyl chloride (4.7 cm^3, 54 mmol) in dichloromethane (80 cm^3) at −60 °C was slowly added a solution of dimethyl sulfoxide (8.3 cm^3, 117 mmol) in dichloromethane (40 cm^3). After stirring at −60 °C for 5 min a cooled solution of alcohol **12** (10 g, 46.7 mmol) in dichloromethane (75 cm^3) was added *via* cannula and the resulting white suspension stirred for 15 min at −60 °C. Triethylamine (35 cm^3, 251 mmol) was added and the mixture stirred for a further 5 min at −60 °C before warming to room temperature. Saturated aqueous ammonium chloride (200 cm^3) was added, the organic phase separated, the aqueous phase extracted with ether (250 cm^3) and the organic extracts dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:4) as eluant gave the *title compound* **13** (7.6 g, 77%) as a colourless oil (Found: M^+, 212.1400. $C_{12}H_{20}O_3$ requires *M*, 212.1412); $[\alpha]_D^{20}$ +28 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} 2720, 1730, 1440, 1370, 1340, 1160, 1050 and 860; δ_H 1.02 (3 H, d, *J* 8, 6-Me), 1.28 (3 H, t, *J* 8, OCH$_2$CH_3), 1.69 (3 H, d, *J* 2, 4-Me), 2.35 (6 H, m, 2-H_2, 3-H_2, 7-H_2), 2.96 (1 H, m, H-6), 4.11 (2 H, q, *J* 8, OCH_2CH$_3$), 5.00 (1 H, d, *J* 11, 5-H) and 9.67 (1 H, t, *J* 3, CHO); *m/z* (CI) 230 (M^+ + 18, 21%), 213 (M^+ + 1, 100) and 195 (89).

Ethyl (4*E*,6*S*,8*E*,10*E*,12*E*)-4,6,12-trimethyltetradecatetra-4,8,10,12-enoate 15

Butyllithium in hexanes (1.55 M; 15.7 cm^3, 24.3 mmol) was added to a solution of redistilled dienyl phosphonate **14**[21] (6.24 g, 27 mmol) in THF (40 cm^3) at −70 °C and the mixture warmed to −40 °C. After stirring for 1 h at this temperature, the suspension was cooled to −70 °C and a cooled solution of aldehyde **13** (4.83 g, 22.8 mmol) in THF (30 cm^3) added *via* a cannula. The mixture was stirred for 1 h at −70 °C, warmed to room temperature, hexamethylphosphoramide (5.94 cm^3, 34 mmol) was added and the mixture stirred for 3 h. Saturated aqueous ammonium chloride (100 cm^3) was added and the mixture extracted with ether (2 × 125 cm^3). The organic extracts were washed with water (100 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure. Chromatography of the residue on base-washed silica using ether–light petroleum (1:20) as eluant gave the *title compound* **15** (5.6 g, 85%) as a colourless oil (Found: M^+, 290.2248. $C_{19}H_{30}O_2$ requires *M*, 290.2246); $[\alpha]_D^{20}$ +8 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} 3020, 1735, 1445, 1370, 1340, 1250, 1155, 985 and 855; δ_H 0.93 (3 H, d, *J* 7.5, 6-Me), 1.25 (3 H, t, *J* 7.5, OCH$_2$CH_3), 1.60 (3 H, s, Me), 1.74 (6 H, overlapping s, d, 2 × Me), 2.05 (2 H, t, *J* 7.5, 7-H_2), 2.25–2.45 (5 H, m, 2-H_2, 3-H_2, 6-H), 4.13 (2 H, q, *J* 7.5, OCH_2CH$_3$), 5.00 (1 H, d, *J* 11, 5-H), 5.58 (2 H, m, vinylic H) and 6.03–6.25 (3 H, m, vinylic H); *m/z* (CI) 308 (M^+ + 18, 1%), 291 (M^+ + 1, 30) and 169 (100).

(4*E*,6*S*,8*E*,10*E*,12*E*)-4,6,12-Trimethyltetradecatetra-4,8,10,12-enoic acid 16

Sodium hydroxide (16 g, 400 mmol) in water (27 cm^3) was added to a solution of ester **15** (5.6 g, 19.3 mmol) in ethanol (70 cm^3) at room temperature. After 4.5 h at this temperature, the mixture was poured into an ice-cold solution of tartaric acid (59 g, 393 mmol) in water (540 cm^3) and extracted with ether (4 × 400 cm^3). The extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in benzene (125 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure to leave the *title compound* **16** (5.21 g, quant.) as a pale brown gum (Found: M^+, 262.1932. $C_{17}H_{26}O_2$ requires *M*, 262.1933); $[\alpha]_D^{20}$ +4.7 (*c* 0.53 in $CHCl_3$); ν_{max}/cm^{-1} 3600–2300, 1705, 1630, 1440, 1380, 1340, 1300, 1210, 1160, 985, 940 and 855; δ_H 0.93 (3 H, d, *J* 7.5, 6-Me), 1.63 (3 H, s, Me), 1.74 (6 H, overlapping s, d, 2 × Me), 2.05 (2 H, t, *J* 7.5, 7-H_2), 2.27–2.52 (5 H, m, 2-H_2, 3-H_2, 6-H), 5.00 (1 H, d, *J* 10, 5-H), 5.59 (2 H, m, vinylic H) and 6.00–6.17 (3 H, m, vinylic H); *m/z* (CI) 280 (M^+ + 18, 4%), 263 (M^+ + 1, 79) and 123 (100).

1-[(4*E*,6*S*,8*E*,10*E*,12*E*)-4,6,12-Trimethyltetradecatetra-4,8,10,12-enoylimidazole 17

1,1′-Carbonyldiimidazole (4 g, 25 mmol) was added to a solution of the acid **16** (5.16 g, 19.7 mmol) in THF (70 cm^3) and the mixture stirred at room temperature for 16 h. The solution was diluted with cold ether (250 cm^3), washed with cold water (125 cm^3), cold brine (125 cm^3) and the aqueous extracts re-extracted with ether (175 cm^3). The organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in benzene (125 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the *title compound* **17** (6.24 g) as a thick brown gum; ν_{max}/cm^{-1} 3030, 1740, 1530, 1475, 1380, 1300, 1215, 1085, 990, 960, 910 and 820; δ_H 0.93 (3 H, d, *J* 10, 6-Me), 1.65 (3 H, s, Me), 1.74 (6 H, overlapping s, d, 2 × Me), 2.07 (2 H, m, 7-H_2), 2.44 (3 H, m, 3-H_2, 6-H), 2.88–3.00 (2 H, m, 2-H_2), 5.00 (1 H, d, *J* 11, 5-H), 5.55 (2 H, m, vinylic H), 5.98–6.23 (3 H, m, vinylic H), 7.08 (1 H, s, 4′-H), 7.45 (1 H, s, 5′-H) and 8.15 (1 H, s, 2′-H); *m/z* (CI) 313 (M^+ + 1, 100%).

(5*R*)-1-Benzoyl-5-benzyl-3-[(4*E*,6*S*,8*E*,10*E*,12*E*)-4,6,12-trimethyl-1-oxotetradecatetra-4,8,10,12-enyl]pyrrolidin-2-one 19

A solution of the 1-benzoylpyrrolidinone **18** (11.3 g, 40.5 mmol) in THF (100 cm^3) at −70 °C was added to a solution of lithium hexamethyldisilazide (40.3 mmol) in THF-hexanes (125 cm^3) at −70 °C. After 1 h, a cooled solution of the amide **17** (6.2 g, 19.9 mmol) was added *via* a cannula and the stirring

continued for 2 h at −70 °C before warming to ambient temperature. After 2 h, the reaction was quenched with saturated aqueous ammonium chloride (130 cm^3) and extracted with ether (3 × 200 cm^3). The organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica using ether–light petroleum (1:6) as eluant gave the *title compound* **19** (9.25 g, 92% from ester **15**), a brown gum, as a mixture of epimers at C-3; $[\alpha]_D^{20}$ +86 (*c* 0.86 in $CHCl_3$); ν_{max}/cm^{-1} 3080, 3060, 3020, 1740, 1715, 1675, 1630, 1600, 1580, 1495, 1450, 1285, 1225, 985, 910, 730, 700 and 655; δ_H 0.85–0.98 (3 H, m, 6′-Me), 1.54–1.85 (9 H, m, 3 × Me), 2.01 (2 H, m, 7′-H_2), 2.13–3.04 (8 H, overlapping m, 4-H_2, 2′-H_2, 3′-H_2, 6′-H, Ph*H*CH), 3.26 (0.5 H, dd, *J* 14, 4, Ph*H*CH), 3.37–3.50 (1 H, m), 3.70 (0.5 H, dd, *J* 10, 8), 4.6 and 4.78 (each 0.5 H, m, 5–H), 4.91 (1 H, m, 5′-H), 5.47–5.70 (2 H, m, vinylic H), 5.97–6.24 (3 H, m, vinylic H) and 7.20–7.67 (10 H, m, ArH); *m*/*z* (CI) 541 (M^+ + 18, 2%), 524 (M^+ + 1, 100), 482 (85) and 105 (75).

(5*R*)-1-Benzoyl-5-benzyl-3-phenylseleno-3-[(4*E*,6*S*,8*E*,10*E*, 12*E*)-4,6,12-trimethyl-1-oxotetradecatetra-4,8,10,12-enyl]pyrrolidin-2-one 20

A solution of the pyrrolidin-2-one **19** (4.6 g, 8.8 mmol) in THF (50 cm^3) at −70 °C was added to a solution of lithium hexamethyldisilazide (9.3 mmol) in THF–hexanes (56 cm^3) at −70 °C *via* a cannula. After 1 h at this temperature, a cooled solution of benzeneselenenyl chloride (2.43 g, 12.7 mmol) in THF (35 cm^3) was added and the mixture stirred for 2 h at −70 °C. The reaction was quenched with saturated aqueous ammonium chloride (75 cm^3) and allowed to reach ambient temperature. Water (40 cm^3) was added and the mixture extracted with ether (1 × 150 cm^3, 2 × 100 cm^3). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica using ether–light petroleum (1:12) as eluant gave the *title compound* **20** (6.16 g, quant.) a yellow gum, a mixture of epimers at C-3; $[\alpha]_D^{20}$ +139 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3060, 3030, 3010, 1730, 1690, 1600, 1450, 1440, 1350, 1280, 1230, 990, 910 and 690; δ_H 0.92 (3 H, m, 6′-Me), 1.53–1.88 (9 H, m, 3 × vinylic Me), 1.88–2.55 (7 H, overlapping m, 4-H_2, 3′-H_2, 6′-H, 7′-H_2), 2.55–2.94 (2.5 H, m), 3.26 (1.5 H, m), 4.54 (1 H, m, 5-H), 4.90 and 4.98 (each 0.5 H, d, *J* 7.5, 5′-H), 5.30–5.70 (2 H, m, vinylic H), 5.96–6.27 (3 H, m, vinylic H) and 7.05–7.68 (15 H, m, ArH); *m*/*z* (CI) 680 (M^+ + 1, 10%) and 524 (100).

(13*E*,16*S*,17*E*)-2-Benzoyl-16,18-dimethyl-10-phenyl[11]-cytochalasa-6(7),13,17-triene-1,21-dione 22

Aqueous hydrogen peroxide (30%; 3.3 cm^3, 29 mmol) in water (14.9 cm^3) and *m*-chloroperoxybenzoic acid (55%; 929 mg, 2.96 mmol) in chloroform (75 cm^3) were added to a solution of the selenide **20** (2 g, 2.75 mmol) in chloroform (135 cm^3) at −50 °C. After 15 min at this temperature, the reaction was warmed to 0 °C, stirred for 5 min then washed with ice-cold saturated aqueous sodium bicarbonate (2 × 60 cm^3), ice-cold water (50 cm^3) and ice-cold brine (40 cm^3). The organic phase was dried (Na_2SO_4) and filtered into hot, argon-degassed, sulfur-free benzene (2 l) and the solution heated under reflux for 8 h. The mixture was then concentrated under reduced pressure and chromatography of the residue using ether–light petroleum (1:9) as eluant gave the *title compound* **22** (0.46 g, 30% from pyrrolidinone **20**) (Found C, 80.8; H, 7.4; N, 2.6. $C_{35}H_{39}NO_3$ requires C, 80.6; H, 7.5; N, 2.7%; Found: M^+, 521.2920. $C_{35}H_{39}NO_3$ requires *M*, 521.2930); $[\alpha]_D^{20}$ +16.5 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3020, 1730, 1705, 1675, 1450, 1370, 1290, 1200, 1100, 975 and 700; δ_H 0.91 (3 H, d, *J* 6, 16-Me), 1.03 (3 H, d, *J* 6, 5-Me), 1.38 (1 H, dt, *J* 20, 2, 19- or 20-H), 1.60 (1 H, q, *J* 11, 15-H), 1.71 (3 H, s, 18-Me), 1.75 (3 H, s, 6-Me), 2.03 (2 H, m, 2 × 19- or 20-H), 2.18 (1 H, m, 15-H), 2.37 (1 H, m, 16-H), 2.51 (1 H, m, 5-H), 2.84 (1 H, m, 8-H), 2.85 (1 H, dd, *J* 13, 6, 10-H), 2.94 (1 H, dd, *J* 6, 2, 4-H), 3.00 (1 H, dd, *J* 13, 2, 10-H), 3.39 (1 H, ddd, *J* 20, 11, 4, 20-H), 4.33 (1 H, m, 3-H), 4.61 (1 H, d, *J* 10, 17-H), 4.98 (1 H, ddd, *J* 17, 11, 4, 14-H), 5.44 (1 H, m, 7-H), 5.89 (1 H, dd, *J* 17, 10, 13-H) and 7.08–7.58 (10 H, m, ArH); *m*/*z* (CI) 539 (M^+ + 18, 4%), 522 (M^+ + 1, 83), 504 (7), 400 (51) and 105 (100). A second product was identified as (13*Z*,16*S*,17*E*)-2-benzoyl-16,18-dimethyl-10-phenyl[11]cytochalasa-6(7),13,17-triene-1,21-dione **23** which, after HPLC using ether–light petroleum (1:12) as eluant, gave ν_{max}/cm^{-1} ($CHCl_3$) 3030, 1738, 1695, 1676, 1602, 1495, 1450, 1371, 1289, 1113, 1003, 909 and 703; δ_H 1.00 (3 H, d, *J* 7.5, 16-Me), 1.23 (3 H, d, *J* 7.5, 5-Me), 1.70 (3 H, s, 18-Me), 1.82 (3 H, s, 6-Me), 1.67–2.63 (8 H, overlapping m, 5-H, 15-H_2, 16-H, 19-H_2, 20-H_2), 2.88 (1 H, dd, *J* 12.5, 5, 10-H), 3.0 (2 H, m, 8-H, 4-H), 3.23 (1 H, dd, *J* 12.5, 7.5, 10-H), 4.23 (1 H, m, 3-H), 4.87 (1 H, d, *J* 10, 17-H), 5.27 (1 H, br s, 7-H), 5.53 (1 H, m, 14-H), 6.07 (1 H, t, *J* 12.5, 13-H) and 7.12–7.62 (10 H, m, ArH); *m*/*z* (CI) 539 (M^+ + 18, 2%), 522 (M^+ + 1, 21) and 174 (100).

(13*E*,16*S*,17*E*)-16,18-Dimethyl-10-phenyl[11]cytochalasa-6(7),13,17-triene-1,21-dione 24

Sodium hydroxide (158 mg, 3.95 mmol) and water (0.18 cm^3) in methanol (8 cm^3) were added to a solution of the Diels–Alder product **22** (98 mg, 0.19 mmol) in methanol–benzene (1:1; 6 cm^3) at room temperature. After 2 h, the mixture was poured into water (40 cm^3) and extracted with ether (3 × 40 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:1) as eluant gave the *title compound* **24** (75 mg, 95%) as a white powder (Found: M^+, 417.2666. $C_{28}H_{35}NO_2$ requires *M*, 417.2668); $[\alpha]_D^{20}$ −110 (*c* 0.37 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3420, 3010, 1695, 1455, 1435, 1385, 1305, 970 and 700; δ_H 0.97 (3 H, d, *J* 8.5, 16-Me), 1.12 (3 H, d, *J* 8.5, 5-Me), 1.75 (7 H, m, 6-Me, 18-Me, 15-H), 1.89 (1 H, dt, *J* 17, 4), 2.11 (2 H, m), 2.24 (1 H, m, 15-H), 2.41 (1 H, m, 16-H), 2.45 (1 H, dd, *J* 13, 8.5, 10-H), 2.52 (1 H, m, 5-H), 2.72 (2 H, m, 4-H, 10-H), 2.84 (1 H, d, *J* 8, 8-H), 3.28 (1 H, m, 3-H), 3.74 (1 H, ddd, *J* 20, 13, 4, 20-H), 4.74 (1 H, d, *J* 13, 17-H), 5.01 (1 H, ddd, *J* 17, 13, 4, 14-H), 5.45 (1 H, s, 7-H), 5.53 (1 H, s, NH), 6.08 (1 H, dd, *J* 17, 8, 13-H) and 7.05–7.33 (5 H, m, ArH); *m*/*z* (CI) 418 (M^+ + 1, 100%).

(13*E*,16*S*,17*R*,18*R*)-17,18-Epoxy-16,18-dimethyl-10-phenyl[11]-cytochalasa-6(7),13-diene-1,21-dione 25

m-Chloroperoxybenzoic acid (7 mg, 85%, 0.035 mmol) in dichloromethane (0.4 cm^3) was added to a solution of the triene **24** (15 mg, 0.035 mmol) in dichloromethane (0.6 cm^3) at −25 °C. After 2 h at this temperature, the solution was allowed to warm to room temperature then poured onto a silica column and eluted with ether–light petroleum (5:1) to provide the *title compound* **25** (14 mg, 92%) as a colourless oil, $[\alpha]_D^{20}$ −118 (*c* 0.26 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3420, 3020, 1700, 1455, 1385, 1305, 980 and 700; δ_H 1.06 (3 H, d, *J* 7.5, 16-Me), 1.17 (3 H, d, *J* 7.5, 5-Me), 1.22 (1 H, m), 1.31 (3 H, s, 18-Me), 1.50 (1 H, m, 16-H), 1.74 (3 H, s, 6-Me), 1.87 (1 H, dd, *J* 20, 5), 2.04 (1 H, m, 15-H), 2.30 (1 H, m, 15-H), 2.44 (3 H, m), 2.51 (1 H, m, 5-H), 2.72 (2 H, m, 8-H, 10-H), 2.91 (1 H, dd, *J* 5, 2.5, 4-H), 3.31 (1 H, m, 3-H), 3.67 (1 H, m, 20-H), 5.20 (1 H, ddd, *J* 15, 12, 3, 14-H), 5.44 (1 H, s, 7-H), 5.49 (1 H, s, NH), 6.40 (1 H, ddd, *J* 15, 11, 2, 13-H) and 7.04–7.33 (5 H, m, ArH); *m*/*z* (EI) 433 (M^+, 4%) and 416 (4).

(6*R*,7*S*,13*E*,16*S*,17*E*)-2-Benzoyl-6,7-dihydroxy-16,18-dimethyl-10-phenyl[11]cytochalasa-13,17-diene-1,21-dione 26

Osmium tetroxide (203 mg, 0.8 mmol) in pyridine (20 cm^3) at −15 °C was added to a solution of the triene **22** (416 mg, 0.8 mmol) in pyridine (40 cm^3) at −15 °C. After 1 h, aqueous sodium metabisulfite (50 cm^3, 20%) was added, and the reaction

allowed to warm to room temperature and stirred for 1 h. Chloroform (100 cm^3) was added and the organic layer washed with water (50 cm^3), brine (50 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:9) as eluant gave recovered starting material **22** (83 mg, 20%) followed by the *title compound* **26** (234 mg, 53%), as a white powder (Found C, 75.8; H, 7.7; N, 2.6. $C_{35}H_{41}NO_5$ requires C, 75.6; H, 7.4; N, 2.5%; Found: M^+, 555.2991. $C_{35}H_{41}NO_5$ requires *M*, 555.2985); $[\alpha]_D^{20}$ −37.5 (*c* 0.9 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3560, 3030, 3010, 1740, 1710, 1675, 1600, 1580, 1450, 1360, 1290, 1180, 1070, 980, 700 and 660; δ_H 0.87 (3 H, d, *J* 7.5, 5-Me), 0.98 (3 H, d, *J* 7.5, 16-Me), 1.20 (3 H, s, 6-Me), 1.64 (2 H, br s, 2 × OH), 1.69 (1 H, q, *J* 11, 15-H), 1.73 (3 H, s, 18-Me), 1.93 (1 H, m, 5-H), 2.31 (4 H, m, 15-H, 19-H_2, 20-H), 2.43 (1 H, m, 16-H), 2.62 (2 H, m, 8-H, 10-H), 2.94 (1 H, dd, *J* 12.5, 2.5, 10-H), 3.12 (1 H, d, *J* 6, 4-H), 3.27 (1 H, d, *J* 10, 7-H), 3.39 (1 H, ddd, *J* 18, 13, 5, 20-H), 4.50 (1 H, dd, *J* 11, 3.5, 3-H), 4.70 (1 H, d, *J* 11, 17-H), 5.15 (1 H, ddd, *J* 16, 11, 4, 14-H), 5.91 (1 H, dd, *J* 16, 10, 13-H) and 7.13–7.60 (10 H, m, Ar-H); *m/z* (CI) 573 (M^+ + 18, 7%), 556 (M^+ + 1, 100) and 538 (M^+ − 17, 44).

The third compound off the column was *(13E,16S,17R,18R)-2-benzoyl-17,18-dihydroxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6,13-diene-1,21-dione* **27** (17 mg, 4%), $[\alpha]_D^{20}$ +8.5 (*c* 0.7 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3620–3220, 3020, 1730, 1700, 1680, 1600, 1450, 1375, 1290, 1215, 1180, 1140, 1110, 980, 910 and 700; δ_H 0.94 (3 H, d, *J* 7.5, 16-Me), 0.99 (3 H, d, *J* 7.5, 5-Me), 1.08 (3 H, s, 18-Me), 1.4 (1 H, m, 16-H), 1.53 (1 H, m), 1.64–1.80 (5 H, m), 1.9 (2 H, m, 15-H_2), 2.32 (1 H, s, exch. D_2O, OH), 2.45 (1 H, m, 5-H), 2.73 (2 H, m, 8-H, 10-H), 3.09 (2 H, m, 4-H, 10-H), 3.50 (1 H, ddd, *J* 18, 8, 2, 20-H), 3.62 (1 H, d, *J* 4.5, 17-H), 4.33 (1 H, m, 3-H), 5.18 (1 H, ddd, *J* 16, 10, 4.5, 14-H), 5.53 (1 H, br s, 7-H), 6.01 (1 H, dd, *J* 16, 10, 13-H) and 7.10–7.65 (10 H, m, ArH); *m/z* (CI) 556 (M^+ + 1, 39%) and 538 (M^+ − 17, 27).

The fourth compound off the column was *(6R,7S,13E,16S,17R,18R)-2-benzoyl-6,7,17,18-tetrahydroxy-16,18-dimethyl-10-phenyl[11]cytochalasa-13-ene-1,21-dione* **28** (76 mg, 16%), as a white powder (Found: M^+, 589.3042. $C_{35}H_{43}NO_7$ requires *M*, 589.3039); $[\alpha]_D^{20}$ −55 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3700–3480, 3020, 1740, 1711, 1679, 1602, 1455, 1286, 1096 and 991; δ_H 0.85 (3 H, d, *J* 7, 5-Me), 0.98 (3 H, d, *J* 7, 16-Me), 1.15 and 1.2 (each 3 H, s, 6-Me, 18-Me), 1.49 (1 H, m, 16-H), 1.72 (1 H, dd, *J* 16, 9), 1.85 (1 H, m, 5-H), 1.90–2.10 (7 H, m), 2.40–2.60 (3 H, m), 2.96 (1 H, dd, *J* 13, 4, 10-H), 3.25 (1H, d, *J* 7, 4-H), 3.46 (2 H, m, 7-H, 20-H), 3.63 (1 H, s, 17-H), 4.44 (1 H, dd, *J* 11, 4, 3-H), 5.35 (1 H, ddd, *J* 17, 13, 4, 14-H), 6.10 (1 H, dd, *J* 17, 10, 13-H) and 7.15–7.70 (10 H, m, ArH); *m/z* (CI) 607 (M^+ + 18, 17%), 590 (M^+ + 1, 34), 572 (M^+ − 17, 60), 556 (21) and 538 (19).

A solution of cooled osmium tetroxide (455 mg, 1.8 mmol) in pyridine (20 cm^3) was added to a solution of the alkene **22** (470 mg, 0.9 mmol) in pyridine (20 cm^3) at −20 °C *via* a cannula. After 0.5 h at −20 °C, aqueous sodium metabisulfite (20%; 80 cm^3) was added and the mixture allowed to warm to ambient temperature and stirred for 1.25 h. After extraction with ethyl acetate (3 × 50 cm^3), the extracts were washed with brine (50 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–light petroleum (1:1) as eluant provided the tetraol **28** (362 mg, 69%) as a white powder, with spectral data as reported above.

(6*R*,7*S*,13*E*,16*S*,17*E*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-6-hydroxy-16,18-dimethyl-10-phenyl[11]cytochalasa-13,17-diene-1,21-dione 29

2,6-Lutidine (0.21 cm^3, 1.8 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.23 cm^3, 1 mmol) were added to a solution of the diol **26** (394 mg, 0.71 mmol) in dichloromethane (12 cm^3) at 0 °C. After 1.5 h at this temperature, water (8 cm^3) was added and the mixture extracted with dichloromethane (1 × 50 cm^3, 2 × 30 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:7) as eluant gave the *title compound* **29** (422 mg, 89%) as a white amorphous solid (Found: M^+, 669.3858. $C_{41}H_{55}NO_5Si$ requires *M*, 669.3849); $[\alpha]_D^{20}$ −4.5 (*c* 0.96 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3610–3390, 3018, 1745, 1710, 1677, 1602, 1450, 1288, 1094, 910 and 836; δ_H −0.08 and 0.00 (each 3 H, s, SiMe), 0.80 (9 H, s, *t*-Bu), 0.86 (3 H, d, *J* 8, 5-Me), 0.97 (3 H, d, *J* 8, 16-Me), 1.05 (3 H, s, 6-Me), 1.6 (1 H, m, 15-H), 1.75 (3 H, s, 18-Me), 2.03 (1 H, m, 5-H), 2.2 (4 H, m, 15-H, 19-H_2, 20-H), 2.46 (1 H, m, 16-H), 2.69 (2 H, m, 8-H, 10-H), 2.9 (1 H, br s, exch. D_2O, OH), 2.90 (1 H, dd, *J* 14, 2, 10-H), 3.00 (1 H, dd, *J* 7, 2.5, 4-H), 3.34 (1 H, m, 20-H), 3.39 (1 H, d, *J* 10, 7-H), 4.54 (1 H, m, 3-H), 4.68 (1 H, d, *J* 10, 17-H), 4.96 (1 H, ddd, *J* 15, 11, 4, 14-H), 5.71 (1 H, dd, *J* 15, 10, 13-H) and 7.15–7.71 (10 H, m, ArH); *m/z* (CI) 687 (M^+ + 18, 1%), 670 (M^+ + 1, 14), 652 (M^+ − 17, 15) and 612 (M^+ − 57, 5).

(7*S*,13*E*,16*S*,17*E*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,17-triene-1,21-dione 30

Triethylamine (0.23 cm^3, 1.7 mmol) and a solution of thionyl chloride (0.06 cm^3, 0.08 mmol) in dichloromethane (0.6 cm^3) were added to a solution of the alcohol **29** (221 mg, 0.33 mmol) in dichloromethane (8 cm^3) at −20 °C. After 0.5 h at this temperature, water (8 cm^3) was added and the mixture extracted with dichloromethane (1 × 30 cm^3, 2 × 20 cm^3). The organic extracts were washed with brine (15 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:20) as eluant gave the *title compound* **30** (183 mg, 85%), as a white powder (Found: M^+, 651.3730. $C_{41}H_{53}NO_4Si$ requires *M*, 651.3744); $[\alpha]_D^{20}$ +45 (*c* 0.84 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3018, 1732, 1709, 1678, 1603, 1452, 1366, 1289, 1075 and 627; δ_H −0.10 (6 H, s, 2 × SiMe), 0.75 (12 H, overlapping s, d, *t*-Bu, 5-Me), 0.94 (3 H, d, *J* 9.5, 16-Me), 1.52–1.83 (5 H, m), 2.02–2.28 (3 H, m), 2.28–2.48 (1 H, m, 16-H), 2.52 (1 H, t, *J* 9.5, 8-H), 2.58 (1 H, dd, *J* 11, 7.5, 10-H), 2.78 (1 H, m, 5-H), 2.95 (2 H, m, 4-H, 10-H), 3.36 (1 H, ddd, *J* 19, 15, 6, 20-H), 3.90 (1 H, d, *J* 9.5, 7-H), 4.40 (1 H, m, 3-H), 4.65 (1 H, d, *J* 11, 17-H), 4.95 (3 H, m, 12-H_2, 14-H), 5.73 (1 H, dd, *J* 15, 9.5, 13-H) and 7.11–7.64 (10 H, m, ArH); *m/z* (EI) 651 (M^+, 0.6%), 594 (M^+ − 57, 43) and 105 (100).

(7*S*,13*E*,16*S*,17*R*,18*R*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-17,18-dihydroxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13-diene-1,21-dione 31

A cooled solution of osmium tetroxide (83 mg, 0.33 mmol) in pyridine (6 cm^3) was added to a solution of the triene **30** (210 mg, 0.33 mmol) in pyridine (14 cm^3) at −25 °C. After 0.5 h at this temperature, aqueous sodium metabisulfite (20% w/v; 23 cm^3) was added and the reaction mixture allowed to warm to room temperature then stirred for 1 h. The mixture was diluted with chloroform (60 cm^3) and the aqueous phase separated and extracted with chloroform (15 cm^3). The organic extracts were washed with water (15 cm^3), brine (15 cm^3), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:1) as eluant gave the *title compound* **31** (166 mg, 75%) as a white amorphous solid (Found C, 71.6; H, 8.4; N, 1.8. $C_{41}H_{55}NO_6Si$ requires C, 71.8; H, 8.1; N, 2.0%; Found: M^+, 685.3788. $C_{41}H_{55}NO_6Si$ requires *M*, 685.3798); $[\alpha]_D^{20}$ +42 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3600–3400, 1760, 1706, 1685, 1602, 1495, 1454, 1367, 1288, 1084, 986, 911, 838 and 791; δ_H −0.05 (6 H, 2 × SiMe), 0.72 (12 H, overlapping s, d, *t*-Bu, 5-Me), 0.94 (3 H, d, *J* 7, 16-Me), 1.10 (3 H, s, 18-Me), 1.41 (1 H, m, 16-H), 1.73–1.97 (5 H, m, 15-H_2, 19-H_2, 20-H), 2.00 (2 H, br s, exch.

D_2O, 2 × OH), 2.40–2.55 (2 H, m, 8-H, 10-H), 2.74 (1 H, m, 5-H), 3.00 (1 H, dd, *J* 13, 4, 10-H), 3.08 (1 H, d, *J* 7, 4-H), 3.4 (1 H, m, 20-H), 3.64 (1 H, s, 17-H), 4.05 (1 H, d, *J* 9, 7-H), 4.41 (1 H, m, 3-H), 4.97 (2 H, m, 12-H_2), 5.18 (1 H, ddd, *J* 16, 11, 6, 14-H), 5.88 (1 H, dd, *J* 16, 10, 13-H) and 7.13–7.60 (10 H, m, ArH); *m/z* (EI) 685 (M^+, 0.5%), 668 ($M^+ - 17$, 1), 628 ($M^+ - 57$, 19), 610 (13) and 105 (100).

(7*S*,13*E*,16*S*,17*R*,18*R*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13-diene-1,21-dione 32

A solution of the diol **31** (192 mg, 0.28 mmol), dimethoxypropane (1.8 cm^3, 14.6 mmol) and toluene-*p*-sulfonic acid (5 mg) in chloroform (8 cm^3) was stirred at room temperature for 5 h. The mixture was then diluted with chloroform (40 cm^3), washed with saturated aqueous sodium bicarbonate (10 cm^3) and brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to leave the acetonide **32** (201 mg, 99%) as a white powder. Chromatography of a small sample using ether–light petroleum (1:5) as eluant gave the *title compound* **32** (Found: M^+, 725.4095. $C_{44}H_{59}NO_6Si$ requires *M*, 725.4111); $[\alpha]_D^{20}$ +64.5 (*c* 0.75 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3020, 1729, 1707, 1681, 1602, 1451, 1372, 1286, 1110, 1068 and 838; δ_H −0.10 (6 H, s, 2 × SiMe), 0.74 (9 H, s, *t*-Bu), 0.82 (3 H, d, *J* 7, 5-Me), 1.01 (3 H, d, *J* 7, 16-Me), 1.11 (3 H, s, 18-Me), 1.27 (1 H, m, 16-H), 1.29 and 1.46 (each 3 H, s, Me), 1.5 (1 H, m), 1.8 (3 H, m), 1.98 (1 H, m, 15-H), 2.57 (1 H, dd, *J* 10, 9, 8-H), 2.74 (1 H, dd, *J* 13, 9, 10-H), 2.82 (1 H, m, 5-H), 2.85 (1 H, dd, *J* 13, 3, 10-H), 2.96 (1 H, dd, *J* 6, 1, 4-H), 3.31 (1 H, dt, *J* 18, 3, 20-H), 3.77 (1 H, s, 17-H), 4.00 (1 H, d, *J* 10, 7-H), 4.46 (1 H, m, 3-H), 4.90 and 5.00 (each 1 H, s, 12-H), 5.12 (1 H, ddd, *J* 15, 11, 5, 14-H), 5.83 (1 H, dd, *J* 15, 10, 13-H) and 7.08–7.60 (10 H, m, ArH); *m/z* (EI) 725 (M^+, 4%), 668 ($M^+ - 57$, 8) and 610 (30).

(7*S*,13*E*,16*S*,17*R*,18*R*,20*R*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl-20-phenylseleno[11]cytochalasa-6(12),13-diene-1,21-dione 33

A solution of lithium diisopropylamide in THF (0.45 cm^3, 0.16 mmol) was added to a solution of the ketone **32** (99 mg, 0.14 mmol) in THF (4 cm^3) at −35 °C. After 0.5 h at this temperature, benzeneselenenyl chloride (66 mg, 0.35 mmol) in THF (1 cm^3) was added and the mixture stirred for a further 1.5 h at −35 °C. Saturated aqueous ammonium chloride (2.5 cm^3) was added and the mixture allowed to warm to room temperature. Water (5 cm^3) was added and the mixture extracted with dichloromethane (3 × 10 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–hexane (1:12) as eluant gave the *title compound* **33** (84 mg, 70%), as a white solid (Found: M^+, 881.3599. $C_{50}H_{63}NO_6{}^{80}SeSi$ requires *M*, 881.3589); $[\alpha]_D^{20}$ +39 (*c* 0.86 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3030, 1717, 1686, 1602, 1451, 1373, 1288, 1263, 1071 and 840; δ_H −0.10 (6 H, s, 2 × SiMe), 0.36 (3 H, d, *J* 7, 5-Me), 0.73 (9 H, s, *t*-Bu), 1.05 (3 H, overlapping s, d, 16-Me, 18-Me), 1.35 (1 H, m, 16-H), 1.39 and 1.52 (each 3 H, s, Me), 1.77–2.11 (4 H, m, 15-H_2, 19-H_2), 2.60 (1 H, t, *J* 8, 8-H), 2.71 (1 H, m, 5-H), 3.04 (2 H, m, 4-H, 10-H), 3.23 (1 H, dd, *J* 13, 4, 10-H), 3.92 (1 H, d, *J* 8, 7-H), 4.02 (1 H, s, 17-H), 4.35–4.42 (1 H, m, 3-H), 4.67 (1 H, d, *J* 7, 20-H), 4.93 and 4.97 (each 1 H, s, 12-H), 5.19 (1 H, ddd, *J* 16, 10, 4.5, 14-H), 5.93 (1 H, dd, *J* 16, 10, 13-H) and 7.15–7.80 (15 H, m, ArH); *m/z* (EI) 881 (M^+, 2%), 824 ($M^+ - 57$, 1), 766 (10). Further elution with ether–light petroleum (1:4) gave recovered starting material **32** (24 mg, 24%).

(7*S*,13*E*,16*S*,17*R*,18*R*,20*R*)-7-*tert*-Butyldimethylsilyloxy-17,18--isopropylidenedioxy-16,18-dimethyl-10-phenyl-20-phenylseleno[11]cytochalasa-6(12),13-diene-1,21-dione 34

To a stirred solution of the *N*-benzoyl cytochalasan **33** (161 mg, 0.18 mmol) in methanol (6 cm^3) at room temperature was added a solution of sodium hydroxide (154 mg, 3.85 mmol) and water (0.19 cm^3) in methanol (4 cm^3). After 3 h at ambient temperature, water (10 cm^3) was added and the mixture extracted with dichloromethane (4 × 15 cm^3). The organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to leave the *title compound* **34** (138 mg, 97%), as a white solid. Chromatography of a sample using ether–light petroleum (1:3) as eluant gave the *title compound* **34** (Found: M^+, 777.3342. $C_{43}H_{59}NO_5{}^{80}SeSi$ requires *M*, 777.3327); $[\alpha]_D^{20}$ −12.5 (*c* 0.63 in $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 3420, 1690, 1381, 1163, 1069, 1000, 980 and 839; δ_H −0.02 and 0.02 (each 3 H, s, SiMe), 0.80 (9 H, s, *t*-Bu), 1.05 (6 H, overlapping s, d, 5-Me, 18-Me), 1.14 (3 H, d, *J* 6, 16-Me), 1.32 (1 H, m, 16-H), 1.49 (6 H, s, 2 × Me), 1.82–2.08 (4 H, m, 15-H_2, 19-H_2), 2.72 (1 H, t, *J* 11, 8-H), 2.78–2.90 (2 H, m, 4-H, 10-H), 3.06 (1 H, m, 5-H), 3.12–3.33 (2 H, m, 3-H, 10-H), 4.06 (2 H, overlapping s, d, 7-H, 17-H), 5.04–5.21 (4 H, m, 12-H_2, 14-H, 20-H), 5.50 (1 H, s, NH), 5.90 (1 H, dd, *J* 16, 11, 13-H) and 7.15–7.60 (10 H, m, ArH); *m/z* (EI) 777 (M^+, 27%), 720 ($M^+ - 57$, 8) and 661 (100).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*)-2-Benzoyl-7-*tert*-butyldimethylsilyloxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,19-triene-1,21-dione 35

Following the procedure outlined for the synthesis of enone **36**, the selenide **33** (20 mg, 0.023 mmol), after chromatography using ether–light petroleum (1:12) as eluant gave the *title compound* **35** (11 mg, 67%) as a colourless oil (Found: M^+, 723.3966. $C_{44}H_{57}NO_6Si$ requires *M*, 723.3955); ν_{max}/cm^{-1} ($CDCl_3$) 3020, 1730, 1684, 1624, 1452, 1376, 1287, 1255, 1221, 1180, 1074 and 839; δ_H −0.08 (6 H, s, 2 × SiMe), 0.60 (3 H, d, *J* 7.5, Me), 0.77 (9 H, s, *t*-Bu), 1.12 (3 H, d, *J* 7.5, Me), 1.42, 1.43 and 1.53 (each 3 H, s, Me), 1.73–1.95 (2 H, m, 15-H, 16-H), 2.18 (1 H, m, 15-H), 2.48–2.60 (2 H, m, 8-H, 10-H), 2.72 (1 H, m, 5-H), 2.97 (1 H, d, *J* 7.5, 4-H), 3.13 (1 H, dd, *J* 12.5, 5, 10-H), 3.68 (1 H, d, *J* 7.5, 17-H), 4.03 (1 H, d, *J* 10, 7-H), 4.53 (1 H, dd, *J* 10, 5, 3-H), 4.93 and 5.00 (each 1 H, s, 12-H), 5.15 (1 H, m, 14-H), 5.78 (1 H, dd, *J* 15, 11, 13-H), 6.40 and 6.75 (each 1 H, d, *J* 16, vinylic H) and 7.27–7.75 (5 H, m, ArH); *m/z* (CI) 741 ($M^+ + 18$, 0.3%), 724 ($M^+ + 1$, 8) and 666 ($M^+ - 57$, 6).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*)-7-*tert*-Butyldimethylsilyloxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,19-triene-1,21-dione 36

Pyridine (0.2 cm^3, 2.5 mmol) and a mixture of water–30% hydrogen peroxide (1:1; 1.5 cm^3) were added to a solution of the selenide **34** (168 mg, 0.22 mmol) in dichloromethane (8 cm^3) at room temperature. After 3 h at this temperature, saturated aqueous ammonium chloride (6 cm^3) was added and the mixture extracted with dichloromethane (3 × 10 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (2:3) as eluant gave the *title compound* **36** (89 mg, 65% from selenide **34**), as a white powder (Found: M^+, 619.3712. $C_{37}H_{53}NO_5Si$ requires *M*, 619.3693); $[\alpha]_D^{20}$ −25 (*c* 0.45 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3420, 3020, 1695, 1625, 1455, 1379, 1298, 1253, 1076 and 839; δ_H 0.00 (6 H, s, 2 × SiMe), 0.80 (9 H, s, *t*-Bu), 1.02 (3 H, d, *J* 7, 5-Me), 1.14 (3 H, d, *J* 7, 16-Me), 1.34 (3 H, s, 18-Me), 1.50 and 1.53 (each 3 H, s, Me), 1.72 (1 H, m, 16-H), 1.96 (1 H, m, 15-H), 2.13 (1 H, m, 15-H), 2.46 (1 H, t, *J* 9, 8-H), 2.51 (1 H, dd, *J* 13, 9, 10-H), 2.70 (1 H, dd, *J* 9, 5, 10-H), 2.85 (1 H, m, 5-H), 3.20 (1 H, dd, *J* 6, 2.5, 4-H), 3.34 (1 H, m, 3-H), 3.87 (1 H, d, *J* 4, 17-H), 4.08 (1 H, d, *J* 9, 7-H), 4.97 and 5.05 (each 1 H, s, 12-H), 5.02 (1 H, m, 14-H), 5.50 (1 H, br s, NH), 5.91 (1 H, dd, *J* 15, 10, 13-H), 6.26 (1 H, d, *J* 16) and 7.12–7.42 (6 H, m); *m/z* (EI) 619 (M^+, 47%), 604 ($M^+ - 15$, 5), 562 ($M^+ - 57$, 52) and 504 (100).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-7-*tert*-Butyldimethylsilyloxy-21-hydroxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,19-trien-1-one 37

Sodium borohydride (10 mg, 0.26 mmol) was added to a solution of the enone **36** (89 mg, 0.14 mmol) and cerium(III) chloride heptahydrate (1.33 g, 3.6 mmol) in methanol (9 cm^3) at 10 °C over 10 min. Water (5 cm^3) was added and the mixture extracted with dichloromethane (3 × 15 cm^3). The organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (3:2) as eluant gave the *title compound* **37** (83 mg, 93%), as a white powder (Found: M^+, 621.3852. $C_{37}H_{55}NO_5Si$ requires *M*, 621.3849); $[\alpha]_D^{20}$ −28 (*c* 0.76 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3680, 3608, 3418, 3020, 1693, 1605, 1460, 1430, 1376, 1256, 1069, 970, 838 and 778; δ_H −0.05 and 0.00 (each 3 H, s, SiMe), 0.84 (9 H, s, *t*-Bu), 1.09 (3 H, d, *J* 7, 5-Me), 1.16 (3 H, d, *J* 7, 16-Me), 1.27 (3 H, s, 18-Me), 1.44 and 1.48 (each 3 H, s, Me), 1.65–1.96 (3 H, m, 15-H, 16-H, OH), 2.08 (1 H, m, 15-H), 2.59 (2 H, m, 4-H, 10-H), 2.86 (1 H, t, *J* 9, 8-H), 2.99 (2 H, m, 5-H, 10-H), 3.30 (1 H, m, 3-H), 3.89 (2 H, m, 7-H, 17-H), 4.24 (1 H, m, 21-H), 4.95 (1 H, m, 14-H), 5.00 and 5.14 (each 1 H, s, 12-H), 5.44 (1 H, dd, *J* 16, 2, 19- or 20-H), 5.48 (1 H, s, NH), 5.65 (1 H, dd, *J* 16, 9, 13-H), 6.47 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.15–7.36 (5 H, m, ArH); *m*/*z* (EI) 621 (M^+, 12%), 604 (M^+ − 17, 12), 603 (23), 564 (M^+ − 57, 19) and 546 (38).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-7-*tert*-butyldimethylsilyloxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,19-trien-1-one 38

Triethylamine (0.1 cm^3, 0.72 mmol), *N*,*N*-dimethylaminopyridine (10 mg, 0.08 mmol) and a solution of acetic anhydride (0.045 cm^3, 0.48 mmol) in dichloromethane (0.45 cm^3) were added to a solution of the alcohol **37** (83 mg, 0.13 mmol) in dichloromethane (3 cm^3) at room temperature. After 2 h, the mixture was diluted with dichloromethane (15 cm^3) and washed with aqueous sodium carbonate solution (10%; 7 cm^3). The aqueous phase was extracted with dichloromethane (2 × 8 cm^3) and the organic extracts washed with brine (8 cm^3), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–hexane (1:2) as eluant gave the *title compound* **38** (72 mg, 81%) as a white amorphous solid (Found: M^+, 663.3949. $C_{39}H_{57}NO_6Si$ requires *M*, 663.3955); $[\alpha]_D^{20}$ −39.6 (*c* 0.82 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3416, 3020, 1743, 1696, 1603, 1374, 1233, 1066 and 838; δ_H −0.05 and −0.01 (each 3 H, s, SiMe), 0.84 (9 H, s, *t*-Bu), 1.06 (3 H, d, *J* 8, 5-Me), 1.09 (3 H, d, *J* 8, 16-Me), 1.23 (3 H, s, 18-Me), 1.44 and 1.47 (each 3 H, s, Me), 1.72 (1 H, m, 16-H), 1.89 (1 H, m, 15-H), 2.05 (1 H, m, 15-H), 2.14 (1 H, m, 4-H), 2.22 (3 H, s, OAc), 2.63 (1 H, dd, *J* 13.5, 11, 10-H), 2.8 (1 H, m, 5-H), 2.91 (2 H, m, 8-H, 10-H), 3.25 (1 H, m, 3-H), 3.89 (2 H, m, 7-H, 17-H), 5.0 (1 H, m, 14-H), 4.98 and 5.15 (each 1 H, s, 12-H), 5.19 (1 H, dd, *J* 16, 2, 19- or 20-H), 5.46 (1 H, s, NH), 5.60–5.72 (2 H, m, 13-H, 21-H), 6.32 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.13–7.42 (5 H, m, ArH); *m*/*z* (EI) 663 (M^+, 8%), 648 (M^+ − 15, 6), 606 (M^+ − 57, 31), 603 (69) and 546 (46).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*R*)-7-*tert*-Butyldimethylsilyloxy-17,18-isopropylidenedioxy-19-methoxy-16,18-dimethyl-10-phenyl[11]-cytochalasa-6(12),13-diene-1,21-dione 39

Following the procedure outlined for the synthesis of the *NH*-lactam **34**, the *N*-benzoyl enone **35** (13 mg, 0.018 mmol) in methanol (1 cm^3) was treated with sodium hydroxide in aqueous methanol to give, after chromatography using ether–light petroleum (1:2) as eluant, the *title compound* **39** (8 mg, 64%), as a white solid; ν_{max}/cm^{-1} ($CHCl_3$) 3421, 1698, 1605, 1455, 1430, 1382, 1290, 1255, 1105, 1066, 1000, 982, 909, 862 and 838; δ_H 0.00 (6 H, s, 2 × SiMe), 0.80 (9 H, s, *t*-Bu), 1.00 and 1.06 (each 3 H, d, *J* 8, Me), 1.24 (3 H, s, 18-Me), 1.37 (1 H, m, 16-H), 1.44 and 1.46 (3 H, s, Me), 1.84–2.04 (3 H, m, 15-H_2, 20-H), 2.44 (1 H, dd, *J* 15, 10, 10-H), 2.62–2.74 (3 H, m, 4-H, 8-H, 10-H), 2.93 (1 H, m, 5-H), 3.37 (2 H, m, 3-H, 20-H), 3.42 (3 H, s, OMe), 3.84 (1 H, s, 17-H), 4.12 (1 H, d, *J* 10, 7-H), 4.22 (1 H, dd, *J* 20, 5, 19-H), 4.94 and 5.04 (each 1 H, s, 12-H), 5.11 (1 H, ddd, *J* 15, 11, 5, 14-H), 5.48 (1 H, br s, NH), 5.94 (1 H, dd, *J* 15, 10, 13-H) and 7.04–7.34 (5 H, m, ArH); *m*/*z* (FAB) 674 (M^+ + 23, 0.4%), 651 (M^+, 2), 636 (M^+ − 15, 1), 594 (M^+ − 57, 6) and 562 (3).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-7-hydroxy-17,18-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-6(12),13,19-trien-1-one 40

A dry solution of tetrabutylammonium fluoride in THF [prepared from commercial material (Aldrich) by drying over $MgSO_4$, filtering onto activated molecular sieves then standing at room temperature under an argon atmosphere for 24 h] (1 M; 0.25 cm^3, 0.25 mmol) was added to the silyl ether **38** (22 mg, 0.033 mmol) and the mixture stirred at room temperature for 2 h. Saturated aqueous ammonium chloride (1 cm^3) was added followed by water (2 cm^3). The mixture was extracted with ethyl acetate (3 × 5 cm^3) and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (3:1) as eluant gave the *title compound* **40** (13 mg, 72%) as a white powder, $[\alpha]_D^{20}$ −39 (*c* 0.4 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3688, 3415, 3020, 1744, 1696, 1604, 1455, 1428, 1375, 1232, 1067, 1017 and 968; δ_H 1.11 and 1.15 (each 3 H, d, *J* 7, Me), 1.24 (3 H, s, 18-Me), 1.44 and 1.48 (each 3 H, s, Me), 1.55–1.84 (3 H, m, OH, 15-H, 16-H), 1.95 (1 H, q, *J* 11, 15-H), 2.16 (4 H, m, 4-H, OAc), 2.57 (1 H, dd, *J* 14, 10, 10-H), 2.77–3.00 (3 H, m, 10-H, 8-H, 5-H), 3.2 (1 H, m, 3-H), 3.79 (1 H, d, *J* 11, 7-H), 3.84 (1 H, d, *J* 4.5, 17-H), 5.14–5.28 (3 H, m, NH, 14-H, 19- or 20-H), 5.45 and 5.48 (each 1 H, s, 12-H), 5.59 (1 H, m, 21-H), 5.78 (1 H, dd, *J* 16, 10, 13-H), 6.36 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.10–7.38 (5 H, m, ArH); *m*/*z* (CI) 550 (M^+ + 1, 2%), 549 (6), 491 (25), 473 (55), 431 (65) and 413 (78).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-17,18-isopropylidenedioxy-16,18-dimethyl-7-(2-trimethylsilylethoxymethoxy)-10-phenyl[11]cytochalasa-6(12),13,19-trien-1-one 41

Diisopropylethylamine (0.15 cm^3, 0.86 mmol) and 2-trimethylsilylethoxymethyl chloride (0.075 cm^3, 0.42 mmol) were added to a solution of alcohol **40** (11 mg, 0.02 mmol) in dichloromethane (0.5 cm^3) at room temperature. After 4 h at this temperature, water (1 cm^3) was added and the mixture was extracted with ethyl acetate (3 × 3 cm^3). The organic extracts were washed with brine (3 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–hexane (1:1) as eluant gave the *title compound* **41** (10 mg, 74%), as a white powder (Found: M^+, 679.3918. $C_{39}H_{57}NO_7Si$ requires *M*, 679.3904); $[\alpha]_D^{20}$ −30.5 (*c* 0.44 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3417, 1743, 1697, 1600, 1460, 1432, 1375, 1233, 1070, 1020, 965, 861 and 837; δ_H 0.00 (9 H, s, 3 × SiMe), 0.9 (2 H, m, CH_2Si), 0.98 (3 H, d, *J* 7, 5-Me), 1.11 (3 H, d, *J* 7, 16-Me), 1.25 (3 H, s, 18-Me), 1.47 and 1.50 (each 3 H, s, Me), 1.74 (1 H, m, 16-H), 1.95 (1 H, q, *J* 12, 15-H), 2.12 (1 H, m, 15-H), 2.20 (1 H, t, *J* 4, 4-H), 2.24 (3 H, s, OAc), 2.73 (2 H, m, 5-H, 10-H), 2.85 (1 H, dd, *J* 14, 5, 10-H), 3.00 (1 H, t, *J* 9, 8-H), 3.3 (1 H, m, 3-H), 3.56 (2 H, m, OCH_2CH_2Si), 3.89 (1 H, s, 17-H), 3.91 (1 H, d, *J* 9, 7-H), 4.53 and 4.69 (each 1 H, d, *J* 8, O*H*CHO), 5.18 (3 H, m, 12-H_2, 14-H), 5.24 (1 H, dd, *J* 16, 3, 19- or 20-H), 5.49 (1 H, br s, NH), 5.69 (1 H, m, 21-H), 5.89 (1 H, dd, *J* 16, 9, 13-H), 6.31 (1 H, dd, *J* 16, 4, 19- or 20-H) and 7.14–7.38 (5 H, m, ArH); *m*/*z* (EI) 679 (M^+, 19%), 664 (M^+ − 15, 6), 637 (12), 619 (62), 562 (42), 533 (31) and 472 (46).

(7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-17,18-dihydroxy-16,18-dimethyl-7-(2-trimethylsilylethoxymethoxy)-10-phenyl[11]-cytochalasa-6(12),13,19-trien-1-one 42

Aqueous hydrogen chloride (1 M; 3 cm^3) was added dropwise to a solution of the acetonide **41** (40 mg, 0.059 mmol) in THF (3 cm^3) and the mixture stirred for 4 h at room temperature. Chloroform (10 cm^3) was added and the solution washed with aqueous sodium carbonate (10%; 5 cm^3). The aqueous phase was extracted with chloroform (2 × 5 cm^3) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica using ether then ethyl acetate as eluant gave recovered starting material **41** (10 mg, 25%) followed by the *title compound* **42** (24 mg, 64%), as a white solid (Found: $M^+ - CH_3$, 624.3360. $C_{35}H_{50}NO_7Si$ requires *M*, 624.3356); $[\alpha]_D^{20}$ −43 (*c* 0.63 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3421, 3020, 1738, 1698, 1605, 1374, 1237, 1070, 1057, 1020, 968, 920, 861 and 839; δ_H 0.00 (9 H, s, 3 × SiMe), 0.83–0.93 (5 H, m, CH_2Si, 5-Me), 1.01 (3 H, d, *J* 9, 16-Me), 1.23 (3 H, s, 18-Me), 1.44 (1 H, m, 16-H), 2.0 (4 H, m, 15-H_2, 2 × OH), 2.15 (1 H, dd, *J* 8, 2, 4-H), 2.27 (3 H, s, OAc), 2.65 (1 H, m, 5-H), 2.79 (2 H, m, 10-H_2), 2.96 (1 H, t, *J* 10, 8-H), 3.27 (1 H, m, 3-H), 3.38–3.68 (3 H, m, OCH_2CH_2Si, 17-H), 3.96 (1 H, d, *J* 10, 7-H), 4.50 and 4.69 (each 1 H, d, *J* 8, OHC*H*O), 5.03 (2 H, m, 12-H_2), 5.22 (2 H, m, 14-H, 19- or 20-H), 5.70–5.85 (1 H, br s, NH), 5.71 (1 H, s, 21-H), 5.83 (1 H, dd, *J* 15, 10, 13-H), 6.30 (1 H, d, *J* 15, 19- or 20-H) and 7.10–7.37 (5 H, m, ArH); *m*/*z* (EI) 624 (M^+ −15, 1%), 611 (M^+ − 18, 4), 580 (4) and 548 (7).

(7*S*,13*E*,16*S*,18*R*,19*E*,21*R*)-21-Acetoxy-18-hydroxy-16,18-dimethyl-7-(2-trimethylsilylethoxymethoxy)-10-phenyl[11]-cytochalasa-6(12),13,19-triene-1,17-dione 43

A solution of dimethyl sulfoxide (0.053 cm^3, 0.75 mmol) in dichloromethane (0.32 cm^3) was added to a solution of oxalyl chloride (0.029 cm^3, 0.33 mmol) in dichloromethane (1 cm^3) at −60 °C. After stirring for 5 min, a cooled solution of the diol **42** (22 mg, 0.034 mmol) in dichloromethane (1.5 cm^3) was added *via* a cannula and the stirring continued for 10 min at −60 °C. Triethylamine (0.2 cm^3, 1.43 mmol) was added, and the mixture stirred for 15 min at −60 °C, warmed to ambient temperature and stirred for 5 min. Saturated aqueous ammonium chloride (3 cm^3) was added and the mixture extracted with ethyl acetate (3 × 5 cm^3). The organic extracts were washed with brine (3 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether–hexane (3:1) as eluant afforded the *title compound* **43** (16 mg, 75%), as a white solid (Found: $M^+ - CH_3$, 622.3226. $C_{35}H_{48}NO_7Si$ requires *M*, 622.3200); $[\alpha]_D^{20}$ −45 (*c* 0.47 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3421, 3020, 1741, 1705, 1455, 1445, 1374, 1232, 1095, 1018, 966, 861 and 838; δ_H 0.00 (9 H, s, 3 × SiMe), 0.82–0.93 (5 H, m, CH_2Si, 5-Me), 1.19 (3 H, d, *J* 7, 16-Me), 1.50 (3 H, s, 18-Me), 1.69 (1 H, br s, OH), 1.99 (1 H, dd, *J* 12, 5, 15-H), 2.15 (1 H, dd, *J* 5, 3, 4-H), 2.29 (3 H, s, OAc), 2.46 (1 H, q, *J* 12, 15-H), 2.60–2.78 (4 H, m, 16-H, 10-H_2, 5-H), 2.92 (1 H, t, *J* 10, 8-H), 3.25 (1 H, m, 3-H), 3.36–3.62 (2 H, m, OCH_2CH_2Si), 3.89 (1 H, d, *J* 10, 7-H), 4.47 and 4.66 (1 H, d, *J* 7, OHC*H*O), 5.30 (2 H, s, 12-H_2), 5.12 (1 H, dd, *J* 16, 2.5, 19- or 20-H), 5.28 (1 H, ddd, *J* 15, 12, 5, 14-H), 5.42 (1 H, s, NH), 5.67–5.78 (2 H, m, 13-H, 21-H), 6.03 (1 H, dd, *J* 16, 2.5, 19- or 20-H) and 7.12–7.38 (5 H, m, ArH); *m*/*z* (EI) 637 (M^+, 0.2%), 622 (M^+ − 15, 1), 609 (M^+ −18, 1), 550 (6) and 520 (8).

Cytochalasin D 3

Water (0.15 cm^3) and aqueous hydrogen fluoride (60%; 0.25 cm^3) were added to a solution of the SEM ether **43** (6 mg, 0.008 mmol) in acetonitrile (1 cm^3) and the mixture stirred at room temperature for 6.5 h. Chloroform (5 cm^3) was added and the mixture washed with aqueous sodium carbonate (10%; 3 cm^3) and brine (3 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–hexane (3:1) as eluant gave cytochalasin D **3** (3 mg, 69%) as a white powder (Found: M^+, 507.2599. $C_{30}H_{37}NO_6$ requires *M*, 507.2621); $[\alpha]_D^{20}$ −7 (*c* 0.4 in dioxane); $[\alpha]_D^{20}$ −28 (*c* 0.33 in $CHCl_3$) [lit.,[23] −7.5 (*c* 0.55 in dioxane)]; authentic sample: −32.5 (*c* 0.35 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3419, 3020, 1742, 1704, 1610, 1495, 1455, 1435, 1374, 1270, 1228, 1120, 1010, 968 and 920; δ_H 0.96 (3 H, d, *J* 7, 5-Me), 1.20 (3 H, d, *J* 7, 16-Me), 1.50 (3 H, s, 18-Me), 1.60–1.90 (2 H, br s, exch. D_2O, 2 × OH), 2.02 (1 H, dd, *J* 13, 4, 15-H), 2.16 (1 H, m, 4-H), 2.27 (3 H, s, OAc), 2.52 (1 H, q, *J* 11, 15-H), 2.63–2.89 (5 H, m, 5-H, 8-H, 10-H_2, 16-H), 3.23 (1 H, m, 3-H), 3.81 (1 H, d, *J* 11, 7-H), 5.14 (2 H, m, 12-H, 19- or 20-H), 5.27–5.40 (2 H, m, 12-H, 14-H), 5.52 (1 H, s, NH), 5.70 (2 H, m, 13-H, 21-H), 6.12 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.10–7.37 (5 H, m, ArH); δ_H (C_5D_5N) 0.87 (3 H, d, *J* 7.5, 5-Me), 1.08 (3 H, d, *J* 7.5, 16-Me), 1.60 (3 H, s, 18-Me), 2.00 (1 H, m, 15-H), 2.43 (3 H, s, OAc), 2.50 (1 H, m, 4-H), 2.72 (2 H, m, 15-H, 16-H), 2.94 (2 H, m, 10-H_2), 3.05 (1 H, m, 5-H), 3.47 (1 H, t, *J* 11, 8-H), 3.65 (1 H, m, 3-H), 4.50 (1 H, d, *J* 11, 7-H), 5.00 (2 H, br s, 2 × OH), 5.14 (1 H, s, 12-H), 5.51 (1 H, s, 12-H), 5.65 (2 H, m, 14-H, 20-H), 6.10 (1 H, m, 21-H), 6.43 (1 H, dd, *J* 15, 11, 13-H), 6.95 (1 H, dd, *J* 17, 4, 19-H), 7.21–7.35 (5 H, m, ArH) and 9.20 (1 H, s, NH); *m*/*z* (FAB) 508 (M^+ + 1, 6%), 490 (2), 430 (14) and 412 (2).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*)-6,7,17,18-Tetrahydroxy-16,18-dimethyl-10-phenyl[11]cytochalas-13-ene-1,21-dione 45

A solution of the bis-acetonide **46** (22 mg, 0.033 mmol) in methanol–aqueous hydrogen chloride (2 M; 5:1; 1.5 cm^3) was heated under reflux for 16 h. After cooling to room temperature, aqueous sodium carbonate (10%; 1 cm^3) was added and the mixture extracted with chloroform (3 × 2 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate as eluant gave the *title compound* **45** (11 mg, 71%), as a colourless oil (Found: M^+, 485.2779. $C_{28}H_{39}NO_6$ requires *M*, 485.2777); $[\alpha]_D^{20}$ −94.7 (*c* 0.87 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3520–3140, 3416, 3140, 1695, 1600, 1455, 1382, 1266, 1115, 984, 896 and 703; δ_H 0.98 and 1.00 (each 3 H, d, *J* 6, Me), 1.10 and 1.20 (each 3 H, s, 6-Me, 18-Me), 1.42 (1 H, m, 16-H), 1.64 (1 H, m), 1.78–2.07 (4 H, m), 2.20 (1 H, m), 2.45 (1 H, dd, *J* 15, 8, 10-H), 2.58 (1 H, t, *J* 10, 8-H), 2.70 (1 H, dd, *J* 15, 6, 10-H), 2.75–3.05 (4 H, br, exch. D_2O, 4 × OH), 2.82 (1 H, d, *J* 7.5, 4-H), 3.38 (1 H, d, *J* 10, 7-H), 3.55 (1 H, m, 3-H), 3.65–3.80 (2 H, m, 17-H, 20-H), 5.3 (1 H, m, 14-H), 6.07 (1 H, dd, *J* 17, 10, 13-H), 6.18 (1 H, br s, NH) and 7.07–7.35 (5 H, m, ArH); *m*/*z* (CI) 503 (M^+ + 18, 15%), 486 (M^+ + 1, 94), 469 (100) and 466 (28).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*)-2-Benzoyl-6,7:17,18-bis(isopropylidenedioxy)-16,18-dimethyl-10-phenyl[11]cytochalas-13-ene-1,21-dione 46

A solution of the alcohol **28** (312 mg, 0.53 mmol), dimethoxypropane (3.5 cm^3, 28.5 mmol) and toluene-*p*-sulfonic acid monohydrate (15 mg, 0.08 mmol) in chloroform (20 cm^3) was stirred at room temperature for 36 h. Work-up as outlined for the acetonide **33** gave the bis-acetonide **46** (371 mg), as a white powder. Chromatography of a sample using ether–light petroleum (1:3) as eluant gave the *title compound* **46** (Found: M^+, 669.3691. $C_{41}H_{51}NO_7$ requires *M*, 669.3665); $[\alpha]_D^{20}$ +32 (*c* 0.9 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 1728, 1708, 1682, 1451, 1381, 1279, 1219, 1161, 1108, 1062, 1030, 1002 and 983; δ_H 0.75 (3 H, d, *J* 7, 5-Me), 1.02 (3 H, d, *J* 7, 16-Me), 1.12 (6 H, s, 2 × Me), 1.25 (1 H, m, 16-H), 1.28, 1.32, 1.43 and 1.47 (each 3 H, s, Me), 1.51 (1 H, m), 1.85 (3 H, m), 2.05 (2 H, m, 5-H, 15-H), 2.53 (1 H, t, *J* 10, 8-H), 2.68 (1 H, dd, *J* 14, 8, 10-H), 2.9 (2 H, m, 4-H, 10-H), 3.36 (1 H, dt, *J* 20, 5, 20-H), 3.72 (1 H, s,

17-H), 3.81 (1 H, d, *J* 10, 7-H), 4.64 (1 H, m, 3-H), 5.16 (1 H, ddd, *J* 15, 10, 5, 14-H), 5.88 (1 H, dd, *J* 15, 10, 13-H) and 7.03–7.70 (10 H, m, ArH); *m/z* (EI) 669 (M^+, 23%) and 105 (100).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,20*R*)-2-Benzoyl-6,7:17,18-bis-(isopropylidenedioxy)-16,18-dimethyl-10-phenyl-20-phenyl-seleno[11]cytochalas-13-ene-1,21-dione 47

Lithium diisopropylamide in THF–hexanes (0.36 M; 3.2 cm^3, 1.15 mmol) was added to a solution of the ketone **46** (706 mg, 1.06 mmol) at −35 °C. After 45 min at this temperature, a cooled solution of benzeneselenenyl chloride (414 mg, 2.16 mmol) in THF (5 cm^3) was added *via* a cannula and the stirring continued at −35 °C for 45 min. Saturated aqueous ammonium chloride (30 cm^3) was added and the mixture allowed to warm to ambient temperature when water (25 cm^3) was added and the mixture extracted with dichloromethane (1 × 50 cm^3, 2 × 30 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using gradient elution with ether–light petroleum (1:6) to (1:4) gave the *title compound* **47** (450 mg, 52%) (Found: M^+, 825.3132. $C_{47}H_{55}NO_7{}^{80}Se$ requires *M*, 825.3144); $[\alpha]_D^{20}$ +34 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 1720, 1715, 1686, 1602, 1454, 1380, 1265, 1223, 1111, 1072, 1005 and 995; δ_H 0.38 (3 H, d, *J* 7.5, 5-Me), 1.04 (3 H, d, *J* 7.5, 16-Me), 1.08, 1.18, 1.27, 1.35 and 1.40 (each 3 H, s, Me), 1.4 (1 H, m, 16-H), 1.50 (3 H, s, Me), 1.90 (2 H, m, 19-H, 15-H), 2.09 (3 H, m, 5-H, 15-H, 19-H), 2.60 (1 H, t, *J* 10, 8-H), 2.97 (1 H, dd, *J* 5, 2.5, 4-H), 3.05 (1 H, dd, *J* 12.5, 10, 10-H), 3.28 (1 H, dd, *J* 12.5, 4, 10-H), 3.67 (1 H, d, *J* 10, 7-H), 4.00 (1 H, s, 17-H), 4.65 (1 H, m, 3-H), 4.75 (1 H, d, *J* 9, 20-H), 5.21 (1 H, ddd, *J* 16, 13, 6, 14-H), 5.92 (1 H, dd, *J* 16, 10, 13-H) and 7.08–7.82 (15 H, m, ArH); *m/z* (EI) 825 (M^+, 14%), 768 (3), 668 (19) and 610 (11).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,20*R*)-6,7:17,18-Bis(isopropyl-idenedioxy)-16,18-dimethyl-10-phenyl-20-phenylseleno[11]-cytochalas-13-ene-1,21-dione 48

Following the procedure outlined above for the preparation of the *NH*-lactam **34**, the *N*-benzoyl cytochalasan **47** (414 mg, 0.5 mmol) in benzene–methanol (3:4; 35 cm^3) gave the lactam **48** (415 mg). Chromatography of a sample using ether–light petroleum (1:1) as eluant gave *title compound* **48** (Found: M^+, 721.2878. $C_{40}H_{51}NO_6{}^{80}Se$ requires *M*, 721.2881); $[\alpha]_D^{20}$ −39.8 (*c* 0.8 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3414, 3020, 1689, 1460, 1438, 1381, 1305, 1246, 1164, 1115, 1073, 1001 and 980; δ_H 1.06 and 1.15 (each 3 H, d, *J* 7.5, 5-Me, 16-Me), 1.27 (3 H, s, Me), 1.3 (1 H, m, 16-H), 1.32, 1.40 and 1.43 (each 3 H, s, Me), 1.49 (6 H, s, 2 × Me), 1.79 (1 H, dd, *J* 17, 1.4, 19-H), 1.96 (2 H, m, 15-H, 19-H), 2.12 (1 H, m, 15-H), 2.40 (1 H, m, 5-H), 2.62 (1 H, dd, *J* 11, 10, 8-H), 2.84 (1 H, dd, *J* 13, 4, 10-H), 2.89 (1 H, dd, *J* 6, 2.8, 4-H), 3.28 (1 H, dd, *J* 13, 10, 10-H), 3.65 (1 H, m, 3-H), 3.79 (1 H, d, *J* 11, 7-H), 4.08 (1 H, s, 17-H), 5.09 (1 H, dd, *J* 6, 1, 20-H), 5.19 (1 H, ddd, *J* 16, 11, 5, 14-H), 5.67 (1 H, s, NH), 5.99 (1 H, dd, *J* 16, 10, 13-H) and 7.17–7.56 (10 H, m, ArH); *m/z* (EI) 721 (M^+, 28%), 706 (M^+ − 15, 4), 685 (1) and 663 (3).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,19*E*)-6,7:17,18-Bis(isopropyl-idenedioxy)-16,18-dimethyl-10-phenyl[11]cytochalasa-13,19-diene-1,21-dione 49

Following the procedure outlined above for the preparation of the enone **36**, the selenide **48** (415 mg, 0.5 mmol), pyridine (0.5 cm^3) and hydrogen peroxide–water (30%; 1:1; 4.5 cm^3) in dichloromethane (20 cm^3) were stirred at room temperature for 4 h to give, after chromatography using ether–light petroleum (3:2) as eluant, the *title compound* **49** (248 mg, 88% from selenide **47**) (Found: M^+, 563.3257. $C_{34}H_{45}NO_6$ requires *M*, 563.3247); $[\alpha]_D^{20}$ −49 (*c* 0.7 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3416, 2251, 1698, 1625, 1455, 1380, 1298, 1253, 1215, 1116, 1077, 1052 and 974; δ_H 0.96 (3 H, d, *J* 7.5, 5-Me), 1.10 (3 H, d, *J* 7.5, 16-Me), 1.25, 1.30, 1.34, 1.36, 1.49 and 1.54 (each 3 H, s, Me), 1.67 (1 H, m, 16-H), 1.97 (1 H, m, 15-H), 2.15 (2 H, m, 5-H, 15-H), 2.40 (1 H, t, *J* 9, 8-H), 2.52 (1 H, dd, *J* 13, 8.5, 10-H), 2.65 (1 H, dd, *J* 13, 6, 10-H), 3.20 (1 H, dd, *J* 8, 2.5, 4-H), 3.59 (1 H, m, 3-H), 3.84 (2 H, overlapping s, d, 7-H, 17-H), 5.03 (1 H, ddd, *J* 16, 11, 4, 14-H), 5.70 (1 H, s, NH), 5.95 (1 H, dd, *J* 16, 9, 13-H), 6.29 (1 H, d, *J* 16, 19- or 20-H) and 7.10–7.38 (6 H, m); *m/z* (CI) 581 (M^+ + 18, 2%), 564 (M^+ + 1, 17), 523 (23) and 506 (100).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Hydroxy-6,7:17,18-bis(isopropylidenedioxy)-16,18-dimethyl-10-phenyl[11]cyto-chalasa-13,19-dien-1-one 50

Following the procedure outlined above for the synthesis of the alcohol **37**, the enone **49** (171 mg, 0.3 mmol), cerium(III) chloride heptahydrate in methanol (0.42 M; 14 cm^3) and sodium borohydride (25 mg, 0.66 mmol) gave, after chromatography using ether–light petroleum (2:1) as eluant, the *title compound* **50** (165 mg, 96%), as a white powder (Found: M^+, 565.3408. $C_{34}H_{47}NO_6$ requires *M*, 565.3403); $[\alpha]_D^{20}$ −102 (*c* 0.77 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3415, 3020, 1694, 1455, 1430, 1381, 1231, 1181, 1116, 1070, 969 and 886; δ_H 1.08 and 1.10 (each 3 H, d, *J* 7, 5-Me, 16-Me), 1.27 and 1.38 (each 6 H, s, 2 × Me), 1.45 and 1.49 (each 3 H, s, Me), 1.68 (1 H, m, 16-H), 1.94 (1 H, q, *J* 11, 15-H), 2.12–2.36 (3 H, m, 5-H, 15-H, OH), 2.59 (2 H, m, 4-H, 10-H), 2.88 (2 H, m, 8-H, 10-H), 3.60 (1 H, d, *J* 10, 7-H), 3.65 (1 H, m, 3-H), 3.88 (1 H, d, *J* 5, 17-H), 4.20 (1 H, t, *J* 2.5, 21-H), 4.99 (1 H, ddd, *J* 15, 11, 4, 14-H), 5.44 (1 H, dd, *J* 16, 2.5, 19- or 20-H), 5.63 (1 H, s, NH), 5.77 (1 H, dd, *J* 15, 10, 13-H), 6.47 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.12–7.36 (5 H, m, ArH); *m/z* (EI) 565 (M^+, 7%), 550 (M^+ − 15, 9), 547 (M^+ − 18, 21), 490 (28) and 474 (15).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-6,7:17,18-bis(isopropylidenedioxy)-16,18-dimethyl-10-phenyl[11]cyto-chalasa-13,19-dien-1-one 51

Following the procedure outlined for the synthesis of the acetate **38**, triethylamine (0.5 cm^3, 3.6 mmol), 4-(*N*,*N*-dimethylamino)pyridine (4.5 mg, 0.037 mmol), acetic anhydride (0.2 cm^3, 2.12 mmol) and the alcohol **50** (185 mg, 0.33 mmol), after 3 h at room temperature and chromatography using ether–light petroleum (2:1) as eluant, gave the *title compound* **51** (161 mg, 81%) as an amorphous powder (Found: M^+, 607.3512. $C_{36}H_{49}NO_7$ requires *M*, 607.3509); $[\alpha]_D^{20}$ −87 (*c* 0.8 in $CHCl_3$); ν_{max}/cm^{-1} ($CDCl_3$) 3414, 2247, 1742, 1698, 1455, 1427, 1375, 1233, 1195, 1117, 1071 and 967; δ_H 0.93 and 1.09 (each 3 H, d, *J* 7, 5-Me, 16-Me), 1.22 and 1.26 (each 3 H, s, Me), 1.39 (6 H, s, 2 × Me), 1.45 and 1.50 (each 3 H, s, Me), 1.68 (1 H, m, 16-H), 1.96 (1 H, q, *J* 11, 15-H), 2.13 (3 H, m, 4-H, 5-H, 15-H), 2.25 (3 H, s, OAc), 2.63–2.94 (3 H, m, 8-H, 10-H_2), 3.59 (1 H, m, 3-H), 3.63 (1 H, d, *J* 11, 7-H), 3.87 (1 H, d, *J* 4.5, 17-H), 5.06 (1 H, ddd, *J* 16, 11, 4, 14-H), 5.17 (1 H, dd, *J* 16, 2, 19- or 20-H), 5.68 (2 H, m, NH, 21-H), 5.80 (1 H, dd, *J* 16, 9, 13-H), 6.35 (1 H, dd, *J* 16, 3.5, 19- or 20-H) and 7.12–7.36 (5 H, m, ArH); *m/z* (EI) 607 (M^+, 1%), 592 (M^+ − 15, 7), 565 (3), 547 (46), 519 (15), 490 (42), 438 (100) and 425 (65).

(6*R*,7*S*,13*E*,16*S*,17*R*,18*R*,19*E*,21*R*)-21-Acetoxy-17,18-dihydroxy-6,7-isopropylidenedioxy-16,18-dimethyl-10-phenyl-[11]cytochalasa-13,19-dien-1-one 52

Toluene-*p*-sulfonic acid monohydrate (22 mg, 0.12 mmol) was added to a solution of the acetate **51** (170 mg, 0.28 mmol) in methanol (16 cm^3) at room temperature. After 8 h at this temperature, water (5 cm^3) was added and the mixture extracted with chloroform (3 × 10 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced

pressure. Chromatography of the residue using ethyl acetate as eluant gave the *title compound* **52** (119 mg, 74%), as a white amorphous powder (Found: M^+, 567.3185. $C_{33}H_{45}NO_7$ requires *M*, 567.3196); $[\alpha]_D^{20}$ −83 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3740–3140, 3416, 1738, 1698, 1455, 1430, 1374, 1235, 1116, 1060, 1020, 1015, 969 and 704; δ_H 0.80 (3 H, d, *J* 7.5, 5-Me), 1.00 (3 H, d, *J* 7.5, 16-Me), 1.20 (6 H, s, 2 × Me), 1.30–1.48 (7 H, m, 16-H, 2 × Me), 1.90–2.15 (4 H, m, 4-H, 5-H, 15-H_2), 2.28 (3 H, s, OAc), 2.58 (2 H, br s, 2 × OH), 2.66–2.90 (3 H, m, 8-H, 10-H_2), 3.56 (2 H, m, 3-H, 17-H), 3.73 (1 H, d, *J* 11, 7-H), 5.10–5.25 (2 H, m, 14-H, 19- or 20-H), 5.70 (1 H, s, 21-H), 5.75 (1 H, dd, *J* 15, 9.5, 13-H), 6.13 (1 H, br s, NH), 6.33 (1 H, dd, *J* 15, 4, 19- or 20-H) and 7.10–7.35 (5 H, m, ArH); *m*/*z* (FAB) 590 (M^+ + 23, 1%), 568 (M^+ + 1, 1) and 550 (M^+ − 17, 10).

(6*R*,7*S*,13*E*,16*S*,18*R*,19*E*,21*R*)-21-Acetoxy-18-hydroxy-6,7-isopropylidenedioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-13,19-diene-1,17-dione 53

Following the procedure outlined for the synthesis of the hydroxyketone **43**, the diol **52** (91 mg, 0.16 mmol), after chromatography using ethyl acetate–petroleum (1 : 1) as eluant, gave the *title compound* **53** (60 mg, 66%) as a white powder (Found: M^+, 565.3022. $C_{33}H_{43}NO_7$ requires *M*, 565.3040); $[\alpha]_D^{20}$ −91 (*c* 0.8 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3626, 3415, 3060, 1725, 1700, 1650, 1580, 1440, 1410, 1360, 1220, 1110, 1070, 1010 and 970; δ_H 0.82 (3 H, d, *J* 7, 5-Me), 1.16 (6 H, overlapping d and s, 16-Me, Me), 1.25 (1 H, s, exch. D_2O, OH), 1.33 (6 H, s, 2 × Me), 1.48 (3 H, s, Me), 1.94–2.12 (3 H, m, 4-H, 5-H, 15-H), 2.28 (3 H, s, OAc), 2.49 (1 H, q, *J* 12.5, 15-H), 2.62–2.85 (4 H, m, 8-H, 10-H_2, 16-H), 3.55 (1 H, m, 3-H), 3.66 (1 H, d, *J* 11, 7-H), 5.06–5.25 (2 H, m, 14-H, 19- or 20-H), 5.68 (1 H, dd, *J* 16, 10, 13-H), 5.73 (2 H, m, 21-H, NH), 6.06 (1 H, dd, *J* 16, 2.5, 19- or 20-H) and 7.12–7.37 (5 H, m, ArH); *m*/*z* (CI) 583 (M^+ + 18, 58%), 566 (M^+ + 1, 88), 548 (M^+ − 17, 54), 506 (31) and 488 (46).

Cytochalasin O 54

The acetonide **53** (89 mg, 0.16 mmol) in methanol–aqueous hydrogen chloride (2 M; 5 : 1; 1.5 cm^3) was heated under reflux for 3 h. After cooling to room temperature, the mixture was diluted with chloroform (15 cm^3) and washed with aqueous sodium carbonate (10%; 8 cm^3). The aqueous layer was extracted with chloroform (2 × 15 cm^3) and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica using ethyl acetate–light petroleum (3 : 1) as eluant gave cytochalasin O **54** (64 mg, 78%), as a white powder (Found: M^+, 525.2730. $C_{30}H_{39}NO_7$ requires *M*, 525.2727); $[\alpha]_D^{20}$ −39 (*c* 0.8 in methanol) [lit.,[15] −39.3 (*c* 1 in methanol)]; ν_{max}/cm^{-1} ($CHCl_3$) 3740–3100, 3416, 1743, 1703, 1604, 1455, 1425, 1375, 1228, 1114, 1009 and 968; δ_H 1.05 (3 H, d, *J* 7.5, 5-Me), 1.19 (3 H, d, *J* 7.5, 16-Me), 1.22 and 1.50 (each 3 H, s, Me), 1.97–2.19 (3 H, m, 4-H, 5-H, 15-H), 2.23 (3 H, s, OAc), 2.44–2.59 (2 H, m, 10-H, 15-H), 2.70–3.30 (3 H, br s, exch. D_2O, 3 × OH), 2.74 (1 H, m, 16-H), 2.88–3.07 (3 H, m, 7-H, 8-H, 10-H), 3.54 (1 H, m, 3-H), 5.15 (1 H, dd, *J* 15, 2, 19- or 20-H), 5.32 (1 H, ddd, *J* 15, 11, 5, 14-H), 5.49 (1 H, m, 21-H), 5.59 (1 H, dd, *J* 15, 9, 13-H), 5.74 (1 H, s, NH), 6.15 (1 H, dd, *J* 16, 3, 19- or 20-H) and 7.10–7.36 (5 H, m, ArH); δ_H (C_5D_5N) 1.07 (3 H, d, *J* 7, 16-Me), 1.18 (3 H, d, *J* 7, 5-Me), 1.47 and 1.59 (each 3 H, s, Me), 2.00 (1 H, m, 15-H), 2.35 (3 H, s, OAc), 2.46 (1 H, m, 4-H), 2.64–2.80 (3 H, m, 5-H, 15-H, 16-H), 2.87 (1 H, dd, *J* 13, 7, 10-H), 2.99 (1 H, dd, *J* 13, 5, 10-H), 3.59 (1 H, t, *J* 9, 8-H), 3.79 (1 H, d, *J* 9, 7-H), 4.00 (1 H, m, 3-H), 5.48 (1 H, m, 14-H), 5.63 (3 H, br s, 3 × OH), 5.68 (1 H, dd, *J* 15, 3, 19-H), 5.97 (1 H, m, 21-H), 6.37 (1 H, dd, *J* 15, 9, 13-H), 7.02 (1 H, dd, *J* 15, 3, 20-H), 7.23–7.38 (5 H, m, ArH) and 9.32 (1 H, s, NH); *m*/*z* (CI) 543 (M^+ + 18, 51%), 526 (M^+ + 1, 51) and 508 (M^+ − 17, 34).

(6*R*,7*S*,13*E*,16*S*,18*R*,19*E*,21*R*)-21-Acetoxy-18-hydroxy-6,7-thiocarbonyldioxy-16,18-dimethyl-10-phenyl[11]cytochalasa-13,19-diene-1,17-dione 55

A solution of synthetic cytochalasin O **54** (3.5 mg, 6.7 μmol) and thiocarbonyldiimidazole (5 mg, 28 μmol) in toluene (1 cm^3) was heated to 80 °C for 3.5 h. After cooling to room temperature the solution was diluted with ethyl acetate (5 cm^3), washed with water (3 cm^3) and the aqueous phase extracted with ethyl acetate (3 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Filtration of the residue through a short plug of silica gel gave the *title compound* **55** (2.5 mg, 66%), as a colourless oil (Found: M^+ + H, 568.2368. $C_{31}H_{38}NO_7S$ requires *M*, 568.2369); ν_{max}/cm^{-1} ($CHCl_3$) 3414, 3020, 1790, 1745, 1707, 1605, 1455, 1370, 1350, 1312, 1231, 1170, 1045, 1010 and 966; δ_H 0.85 and 1.22 (each 3 H, d, *J* 7.5, 5-Me, 16-Me), 1.40 and 1.53 (each 3 H, s, Me), 2.08 (1 H, dd, *J* 11, 4, 15-H), 2.24 (1 H, m, 4-H), 2.35 (3 H, s, OAc), 2.49 (1 H, q, *J* 11, 15-H), 2.68–3.03 (5 H, m, 5-H, 16-H, 8-H, 10-H_2), 3.54 (1 H, m, 3-H), 4.22 (1 H, d, *J* 11, 7-H), 5.17 (1 H, dd, *J* 17, 2, 19- or 20-H), 5.30 (1 H, m, 14-H), 5.63 (1 H, dd, *J* 15, 10, 13-H), 5.77 (1 H, m, 21-H), 5.96 (1 H, br s, NH), 6.06 (1 H, dd, *J* 17, 2, 19- or 20-H) and 7.16–7.42 (5 H, m, ArH); *m*/*z* (FAB) 568 (M^+ + 1, 25%), 550 (M^+ − 17, 7) and 490 (30).

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