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The Pd-Catalyzed Alder–Ene Reactions of *N*-Protected and Propargylated 1-Amino-2-aryl-2-cyclohexenes as a New Route to C3a-Arylhexahydroindoles: Towards the Total Synthesis of Tazettine

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A series of *N*-protected and propargylated 1-amino-2-aryl-2-cyclohexenes (**4**) has been prepared. Several of these have been shown to undergo an intramolecular Alder–ene reaction in the presence of palladium acetate and the ligand BBEDA to afford C3a-arylhexahydroindoles of the general form **1**. Certain of these products may serve as precursors to the alkaloid tazettine (**2**).

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Introduction

The C3a-arylhexahydroindole unit (**1**, Fig. 1) is the key substructure encountered in a number of *Amaryllidaceae* alkaloids including *Sceletium*-type systems such as mesembrine,[1] the crinines,[2] and tazettine (**2**).[3] As a consequence various methods have been established for the synthesis of this important structural motif although, partly because of the presence of a quaternary carbon centre (C3a), most of these involve relatively complex reaction sequences.[2c,4] In connection with our continuing interest in the synthesis of *Amaryllidaceae* alkaloids,[2f,5] we have been seeking to develop abbreviated total syntheses of tazettine (**2**) and related systems such as macronine[6] and pretazettine.[7] To that end, we sought to establish concise new routes to C3a-arylhexahydroindoles and now report on the successful identification of one.

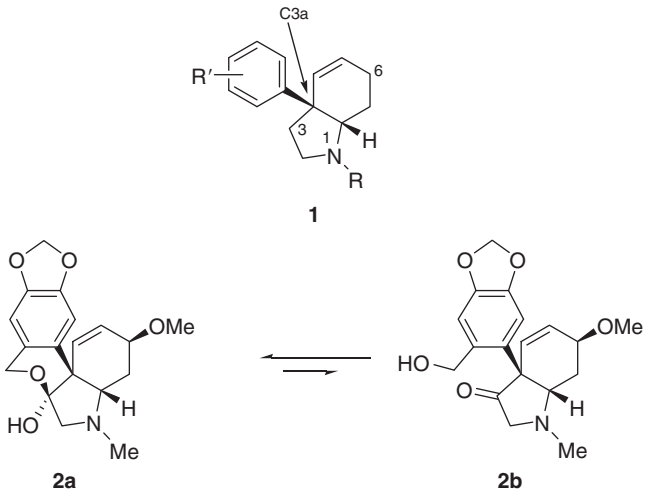

Fig. 1. Structure of tazettine (**2a**) and its ring-opened isomer (**2b**).

Results and Discussion

The key feature of the present approach to the target structure **1** is shown in Fig. 2 and involves the conversion, by an intramolecular Alder–ene (IMAE) reaction, of an *N*-protected and propargylated 1-amino-2-aryl-2-cyclohexene of the general form **3** into a C3a-arylhexahydroindole **4** (corresponding to a protected form of **1**) incorporating the required Δ^4-double bond as well as an exocyclic one at C3. Provided the latter alkene could be oxidatively cleaved in a selective manner, this moiety should serve as a precursor to a carbonyl or hydroxy group that is often encountered at C3 in the abovementioned natural products. Given the geometrical requirements of the IMAE reaction (Fig. 2) the nature of the protecting group, P, at the nitrogen in

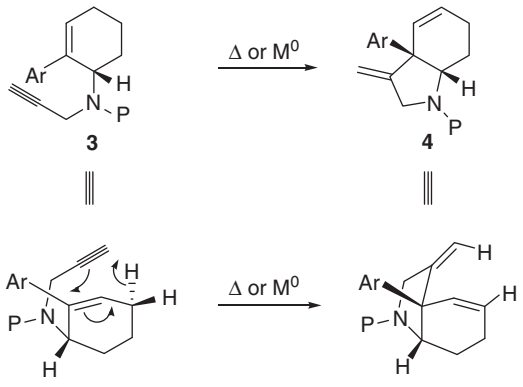

Fig. 2. Proposed synthesis of C3a-arylhexahydroindoles via an IMAE reaction.

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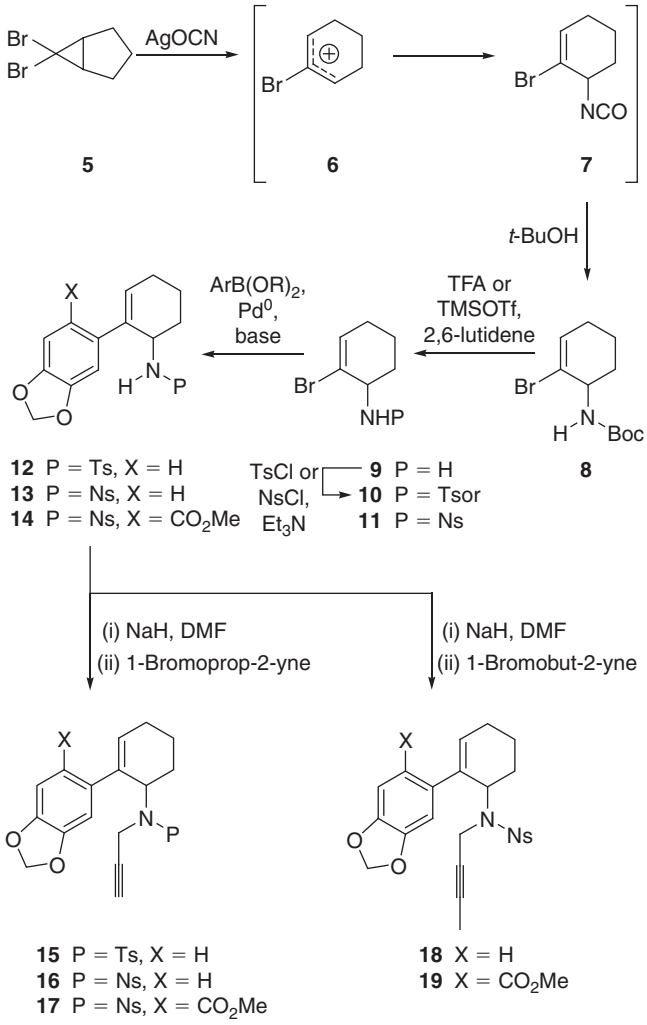
substrate **3** will be crucial to success. In particular, this group must allow the nitrogen and its substituents to assume a tetrahedral geometry and, thereby, the alkyne to interact in the necessary fashion with the cyclohexene double bond and the associated allylic methylene unit. In principle, the IMAE reaction could be promoted thermally or by using a transition metal such as palladium (in a low valent state).[8] In this context it should be noted that Nishimata and Mori[2a] have exploited a thermally induced intramolecular carbonyl–ene reaction of a cyclohexenylamine incorporating an acetaldehyde residue on nitrogen to prepare (+)-crinamine and (+)-pretazettine. However, temperatures in the range of 230–240°C were required to effect the required ene reaction while treatment of the same substrate (at ~0°C) with $SnCl_2$ led to an undesired tricyclic species.

Of course, the utility of the process shown in Fig. 2 will be dependent upon how readily, or otherwise, substrates of the general form **3** can be obtained. The approach we have used to prepare such systems is shown in Scheme 1 and utilizes the electrocyclic ring-opening of the ring-fused *gem*-dibromocyclopropane **5** as the key step in forming the required cyclohexenylamine unit.[9] Thus, as we have reported earlier,[10] treatment of the readily available compound **5** with silver cyanate effected the desired ring-opening process and the



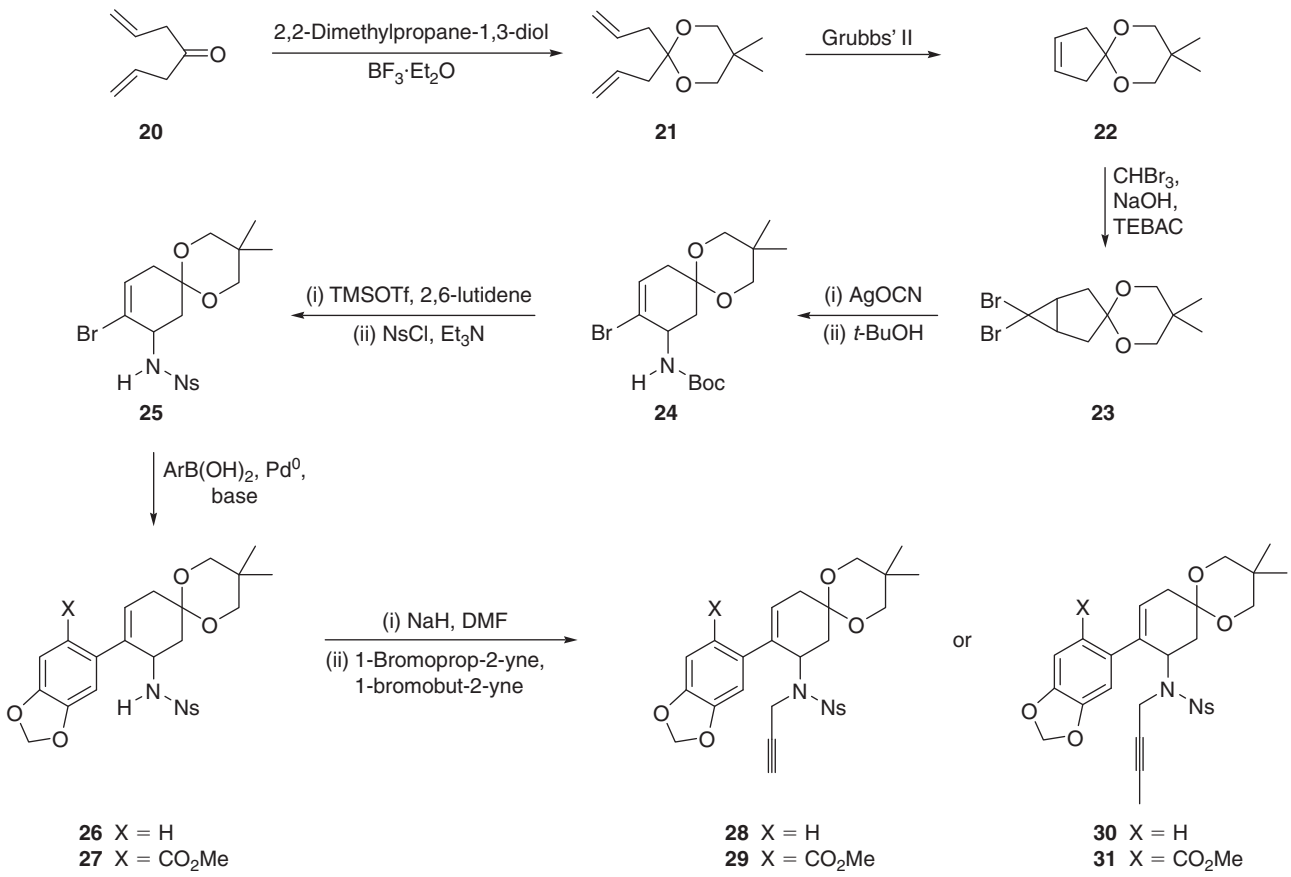
Scheme 1.

π-allyl cation **6** so-formed was intercepted by the nitrogen terminus of the cyanate anion to afford the allylic isocyanate **7**. This last species was itself trapped with added *t*-butanol to afford the Boc-protected primary amine **8** which was obtained in 79% yield. Since Boc-protection of nitrogen results in a planar geometry of substituents attached to this heteroatom[11] this was considered to be an unsuitable protecting group for the substrate **3** to be engaged in the IMAE reaction. Accordingly, the Boc-group within compound **8** was cleaved using trimethylsilyl trifluoromethanesulfonate (TMSOTf) in the presence of 2,6-lutidene[12] or trifluoroacetic acid (TFA) and the free amine **9** obtained after aqueous work-up was treated with either *p*-toluenesulfonyl chloride (TsCl) or *o*-nitrobenzenesulfonyl (nosyl) chloride (NsCl) in the presence of triethylamine and thereby afforded the corresponding sulfonamide **10** (86% from **8**) or **11** (87% from **8**). The sulfonamide-based protecting group was chosen because of the likelihood of the associated nitrogen assuming a geometry[13] that would allow for the desired cyclization reaction. The nosyl protecting group was also considered a particularly attractive one because of the ease with which it can be removed using the phenylthiolate anion.[14]

Suzuki–Miyaura cross-coupling[15] of the cycloalkenyl bromides **10** and **11** with either commercially available 3,4-methylenedioxyphenylboronic acid or the readily prepared methyl 6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzo[*d*][1,3]dioxole-5-carboxylate[5a] resulted in the expected cyclohexenes **12** (78%), **13** (77%), or **14** (69%) incorporating the 3,4-methylenedioxyphenyl moiety commonly encountered in the target alkaloids. In addition, the last of these coupling products contains a suitably positioned carbomethoxy group that could ultimately be converted into the hydroxymethyl unit required for the formation of the lactol residue embodied within tazettine (see conversion **2a** → **2b**). Installation of the pivotal propargyl group at nitrogen within compounds **12**–**14** was readily achieved by their successive treatment with sodium hydride and then propargyl bromide. In this way three of the substrates, **15** (89%), **16** (91%), and **17** (80%), required for the IMAE reaction were obtained. The spectroscopic data derived from these compounds were in complete accord with the assigned structures.

Since our preliminary studies on the IMAE reaction of terminal alkynes **15**–**17** revealed that they also undergo a competitive dimerization reaction (see below), the 'methyl-capped' analogues **18** and **19**, which would be incapable of engaging in this undesired side reaction, were prepared. This was readily achieved by successive treatment of the nosyl-protected precursors **13** and **14** with sodium hydride followed by 1-bromobut-2-yne. By such means the substrates **18** and **19** required for the IMAE reaction were obtained in 86% and 83% yields, respectively.

Given that many of the target alkaloids incorporate oxygen at C6 within the C3a-arylhexahydroindole subunit, we sought to prepare substrates for the IMAE reaction that acknowledged the presence of such functionality. The reaction sequence used for this purpose is shown in Scheme 2 and started with the conversion, under standard conditions, of readily accessible diallyl ketone **20**[16] into the corresponding ketal **21** (91%). This particular ketal derivative was employed because it was significantly less volatile (and therefore much more easily handled) than, for example, the corresponding ethylene ketal. Treatment of a dichloromethane solution of compound **21** with 2 mol-% of Grubbs' II (second generation) catalyst[17] resulted in an efficient ring-closing metathesis reaction and thus provided the



Scheme 2.

cyclopentene **22** in 95% yield. Subjection of alkene **22** to reaction with dibromocarbene, generated under Makosza conditions[18] from bromoform and sodium hydroxide in the presence of the phase-transfer catalyst triethylbenzyl ammonium chloride (TEBAC), gave the anticipated cyclopropane **23** in 67% yield. Following the protocols used earlier,[10] compound **23** was treated successively with silver cyanate and *t*-butanol to give the Boc-protected cyclohexenylamine **24** in 73% yield. Cleavage of the Boc-group within the latter compound and reaction of the resulting free amine with nosyl chloride in the presence of triethylamine then gave the sulfonamide **25** in 72% yield (from **24**). Cross-coupling of compound **25** with the same pair of aryl boronic acids used earlier gave the anticipated products **26** and **27** in yields of 81% and 68%, respectively.

Finally, successive treatment of these cross-coupling products with sodium hydride followed by either propargyl bromide or 1-bromobut-2-yne gave either alkynes **28** (89%) and **29** (74%) or their 'methyl-capped' equivalents **30** (85%) and **31** (96%), respectively. Once again, the spectroscopic data obtained on compounds **28**–**31** were in complete accord with the assigned structures. Further support for these assignments derives from a single-crystal X-ray analysis of sulfonamide **28**. The *ORTEP* diagram so-obtained is presented in Fig. 3 while further details are included in the Experimental section. Significantly, this analysis reveals that, in the solid state at least, compound **28** possesses a pyramidalized geometry at nitrogen and, as a partial consequence, the alkynyl and cyclohexenyl residues appear reasonably well aligned for participation in the anticipated IMAE reaction.

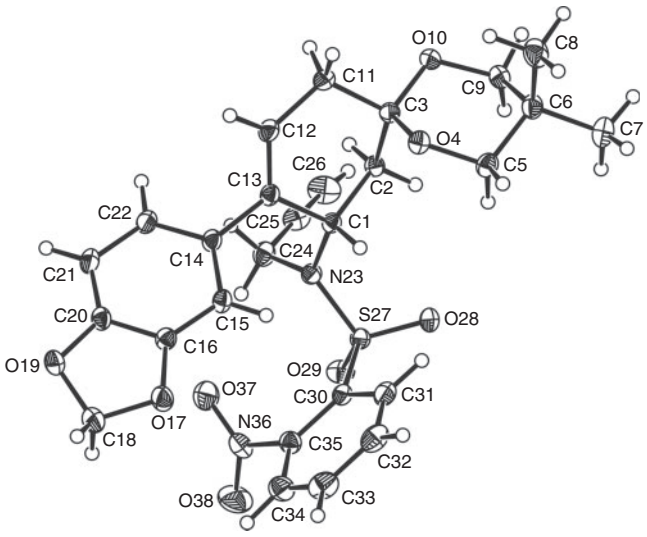
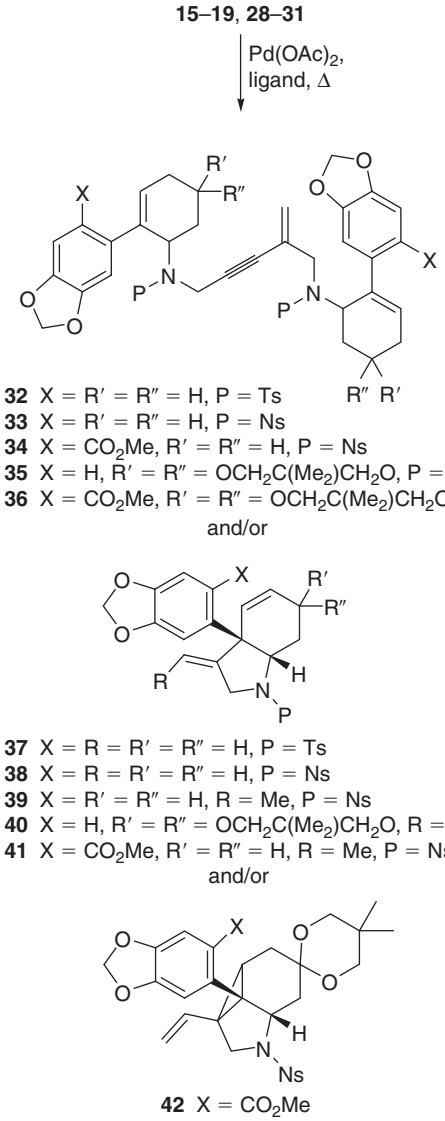


Fig. 3. *ORTEP* diagram derived from the single-crystal X-ray analysis of compound **28** (CCDC 790929) with labelling of non-hydrogen atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

With compounds **15**–**19** and **28**–**31** to hand, their capacities to engage in the pivotal IMAE reaction could be investigated. To such ends we subjected these substrates to conditions used by Trost and Pedregal (Scheme 3).[19] Specifically, each was treated with $Pd(OAc)_2$ and the strong σ-donating ligand *N*,*N*′-bis(benzylidene)ethylenediamine (BBEDA) (~5 mol-% of



32 X = R′ = R″ = H, P = Ts
33 X = R′ = R″ = H, P = Ns
34 X = CO_2Me, R′ = R″ = H, P = Ns
35 X = H, R′ = R″ = $OCH_2C(Me_2)CH_2O$, P = Ns
36 X = CO_2Me, R′ = R″ = $OCH_2C(Me_2)CH_2O$, P = Ns

and/or

37 X = R = R′ = R″ = H, P = Ts
38 X = R = R′ = R″ = H, P = Ns
39 X = R′ = R″ = H, R = Me, P = Ns
40 X = H, R′ = R″ = $OCH_2C(Me_2)CH_2O$, R = Me, P = Ns
41 X = CO_2Me, R′ = R″ = H, R = Me, P = Ns

and/or

42 X = CO_2Me

Scheme 3.

each) or Ph_3P in either 1,2-dichloroethane (DCE), benzene, or toluene. The outcomes of the relevant experiments are shown in Table 1. Thus, for example, heating a solution of substrate **15**, $Pd(OAc)_2$, and BBEDA in DCE for 2 h at 56°C (Entry 1, Table 1) afforded the hoped for C3a-arylhexahydroindole **37** (26%) but the major product of reaction (60%) was a species tentatively assigned as the dimeric compound **32**. These two products could be separated by flash chromatographic methods and the former (**37**) was subjected to comprehensive spectroscopic characterization and its structure finally confirmed by a single-crystal X-ray analysis (see Fig. 4 and the Experimental section for details). The structure of compound **32** follows from the similarity of its ^1H NMR spectrum with that derived from a related but more tractable compound for which comprehensive spectroscopic characterization could be undertaken (see below).

Subjection of the *N*-nosyl analogue, **16**, of compound **15** to analogous cyclization conditions (Entry 2, Table 1) resulted in essentially the same outcome, namely the co-production of a ~2:1 mixture of the chromatographically separable dimer **33** (66%) and the desired C3a-arylhexahydroindole **38** (26%). The mass spectrometric data obtained on compound **33** clearly established it was a dimeric form of substrate **16** while the

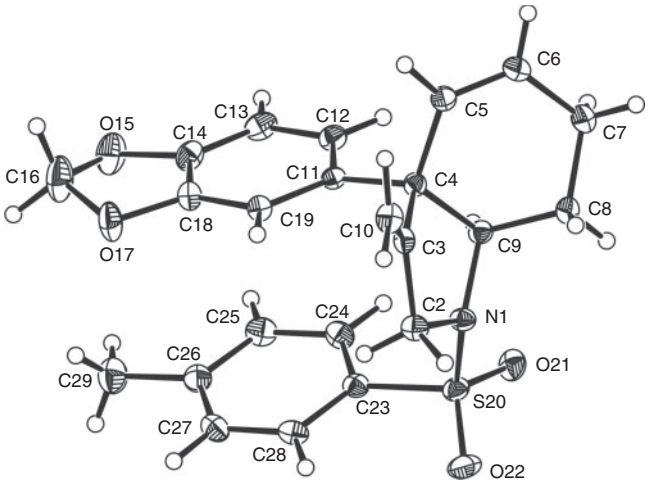


Fig. 4. *ORTEP* diagram derived from the single-crystal X-ray analysis of compound **37** (CCDC 790930) with labelling of non-hydrogen atoms (illustrated enantiomer opposite to that shown in Scheme 3). Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

Table 1. Outcomes of subjecting compounds 15–19 and 28–31 to reaction with $Pd(OAc)_2$ in the presence of *N*,*N*′-bis(benzylidene)ethylenediamine (BBEDA) or Ph_3P

Entry	Substrate	Reaction conditions	Product(s) (% yield)
1	**15**	DCE, 56°C, 2 h, ligand BBEDA	**32** (60) **37** (26)
2	**16**	DCE, 56°C, 4 h, ligand BBEDA	**33** (66) **38** (26)
3	**17**	C_6H_6, 80°C, 1 h, ligand Ph_3P	**34** (47)
4	**18**	C_6H_6, 80°C, 7 h, ligand BBEDA	**39** (94)
5	**19**	Toluene, 110°C, 6 h, ligand BBEDA	**41** (55)
6	**28**	C_6H_6, 80°C, 2 h, ligand Ph_3P	**35** (53)
7	**29**	C_6H_6, 80°C, 2 h, ligand Ph_3P	**36** (72)
8	**30**	C_6H_6, 80°C, 5 h, ligand BBEDA	**40** (100)
9	**31**	Toluene, 110°C, 5 h, ligand BBEDA	**42** (92)

'doubling up' of signals in the ^{13}C NMR spectrum suggested it comprised a ~1:1 mixture of diastereoisomers, as might be expected for a product arising from the coupling of the racemic form of two monomeric units incorporating a single centre of chirality. While the two acetylenic units of monomer **16** could be joined in two distinct ways, so as to produce either the illustrated terminal alkene or the isomeric internal one, work by Yang and Nolan[20] suggests that the process leading to the former type of dimer often predominates. An inspection of the ^1H NMR spectrum of compound **33** revealed two one-proton resonances at δ_H 5.45 and 5.27 suggestive of the presence of hydrogens attached to a terminal carbon–carbon double bond. Such spectroscopic features and the literature precedent mentioned above form the basis for the illustrated structural assignments of the dimeric compounds shown in Scheme 3.

In slight contrast to the outcome of the reaction represented in Entry 2 of Table 1, treatment of the carbomethoxy-substituted system **17** with $Pd(OAc)_2$ and Ph_3P in refluxing benzene for 1 h (Entry 3, Table 1) resulted in the exclusive formation of the corresponding dimer **34**, although this was only isolated in 47% yield.

The dimerization process described above could be prevented by using the 'methyl-capped' system **18** (Entry 4, Table 1) and then the IMAE reaction proceeded very effectively and the desired C3a-arylhexahydroindole **39** was generated in 94% yield. This cyclization product was obtained as a single geometric isomer and, consistent with the likely mechanism of the reaction (see Fig. 2), the illustrated *Z*-configuration about the exocyclic double bond was established by single-crystal X-ray analysis (see Experimental section for details).

When the carbomethoxy-substituted analogue, **19**, of compound **18** was subjected to the same cyclization conditions as described immediately above no reaction was observed. Such an outcome may be attributed to the more sterically congested nature of compound **19**. Accordingly, a solution of the same substrate, $Pd(OAc)_2$, and BBEDA in toluene was heated at reflux and after 6 h complete consumption of the starting material was observed. Upon work-up product **41** was obtained in 55% yield. The structure of compound **41** follows from the derived spectroscopic data.

In keeping with earlier observations, when the terminal alkynes **28** and **29** were treated with $Pd(OAc)_2$ and Ph_3P at elevated temperatures (Entries 6 and 7, Table 1), the corresponding dimers, **35** (53%) and **36** (72%), respectively, were obtained, again as mixtures of diastereoisomers but this time as the only isolable products of the reaction. In pleasing contrast, when the methyl-capped analogue, **30**, of compound **28** was reacted in the same way (Entry 8, Table 1), the C3a-arylhexahydroinole **40** was obtained in quantitative yield. A less satisfying observation was that analogous treatment of the carbomethoxy-substituted congener, **31**, of substrate **30** gave (Entry 9, Table 1) the cyclopropane-annulated product **42** (92%), the structure of which was established by single-crystal X-ray analysis (Fig. 5).

Presumably, this cyclopropane-annulated hexahydroindole arises through participation of the initially formed (and desired) C3a-arylhexahydroindole in a secondary IMAE reaction involving the ethylidene and *endo*-cyclic alkene units. Attempts to suppress this secondary process by using milder reaction conditions have not been effective thus far.

Conclusions

The work presented here demonstrates that *N*-protected and propargylated 1-amino-2-aryl-2-cyclohexenes of the general form **3** are readily obtained through reaction sequences involving initial silver cyanate-promoted electrocyclic ring-opening of 6,6-dibromobicyclo[4.1.0]hexane derivatives. Furthermore, certain of these cyclohexenes participate, under relatively mild conditions, in Pd^0-catalyzed IMAE reactions and thereby affording C3a-arylated hexahydroindoles **4**, some of which may serve as precursors to various *Amaryllidaceae* alkaloids including tazettine **2**. Two (undesirable) processes that can compete with the IMAE reaction have been identified. One of these involves the dimerization of those substrates, **3**, that incorporate a terminal alkyne residue but this is readily prevented by employing 'methyl-capped' propargyl groups. The other process appears to involve a second ene reaction that converts the initially formed C3a-arylhexahydroindole into a cyclopropane-containing isomer. This secondary reaction takes place at the higher temperatures required to promote the initial IMAE reaction of sterically congested substrates.

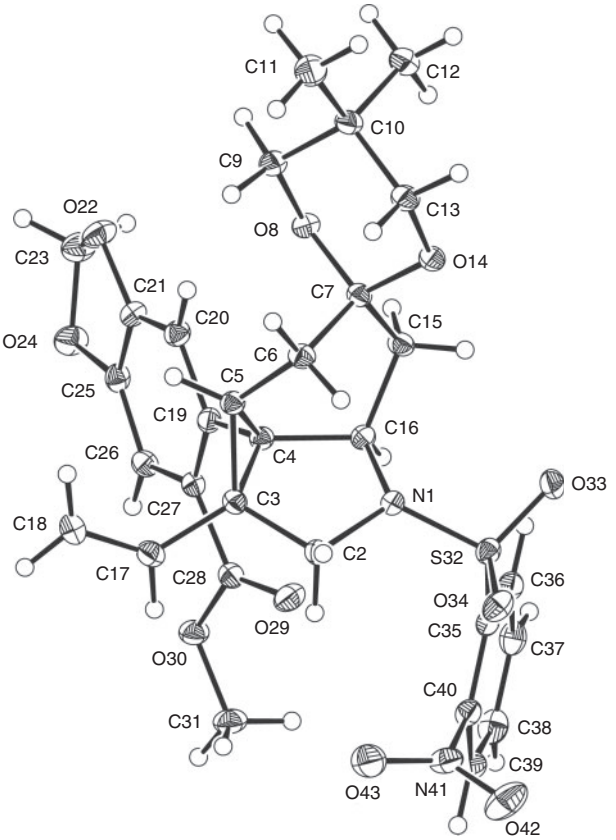


Fig. 5. *ORTEP* diagram derived from the single-crystal X-ray analysis of compound **42** (CCDC 790932) with labelling of non-hydrogen atoms (illustrated enantiomer opposite to that shown in Scheme 3). Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

Experimental

General Experimental Procedures

Proton (^1H) and carbon (^{13}C) NMR spectra were recorded on a Varian Gemini 300 machine (operating at 300 and 75 MHz for ^1H and ^{13}C spectra, respectively), a Varian MR400 instrument (operating at 400 and 100 MHz for ^1H and ^{13}C spectra, respectively), or a Varian VXR500 machine with an

Innova console (operating at 500 and 125 MHz for ^{1}H and ^{13}C spectra, respectively). Unless otherwise specified, spectra were acquired at 20°C in deuterochloroform ($CDCl_3$) that had been stored over anhydrous sodium carbonate. Chemical shifts are recorded as δ values in parts per million [ppm]. Infrared spectra (ν_{max}) were normally recorded on a Perkin–Elmer 1800 Series FTIR Spectrometer and samples were analyzed as thin films on KBr plates (for liquids) or as a KBr disk (for solids). Low-resolution electrospray ionization (ESI) mass spectra were recorded in positive-ion mode on a Micromass–Waters LC-ZMD single quadrupole liquid chromatograph–mass spectrometer while low- and high-resolution electron impact (EI) mass spectra were recorded on a VG Fisions AUTOSPEC three-sector, double-focussing instrument. Melting points were measured on a Stanford Research Systems Optimelt-Automated Melting Point System and are uncorrected. Analytical TLC was performed on aluminium-backed 0.2 mm thick silica gel 60 F254 plates as supplied by Merck. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included a mixture of vanillin/sulfuric acid/ethanol (1 g/1 g/18 mL) or phosphomolybdic acid/ceric sulphate/conc. sulfuric acid/water (37.5 g/7.5 g/37.5 g/720 mL). The retardation factor (R_F) values cited here have been rounded to the first decimal point. Flash chromatographic separations were carried out following protocols defined by Still et al.[21] with silica gel 60 (40–63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials and reagents were generally available from the Sigma–Aldrich, Merck, TCI, Strem, or Lancaster Chemical Companies and were either used as supplied or, in the case of liquids, distilled when required. Drying agents and other inorganic salts were purchased from the AJAX, BDH, or Unilab Chemical Companies. Tetrahydrofuran (THF), dichloromethane, acetonitrile, and benzene were dried using a Glass Contour solvent purification system that is based upon a technology originally described by Grubbs et al.[22] Where necessary, reactions were performed under a nitrogen or argon atmosphere.

Specific Synthetic Procedures and Product Characterization

*Compound **8***

A magnetically stirred mixture of compound **5**[10a] (4.50 g, 18.8 mmol) and silver cyanate (3.23 g, 21.6 mmol) in anhydrous 1,4-dioxane (38 mL) was heated at 105°C under an atmosphere of nitrogen for 4 h and then *t*-butanol (4.7 mL) was added and the ensuing mixture heated at the same temperature for a further 18 h. The resulting slurry was cooled and then filtered through a pad of Celite that was washed with CH_2Cl_2 (200 mL). The combined filtrates were concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/19 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/4 v/v ethyl acetate/hexane), the *title compound **8*** (4.11 g, 79%) as a white, crystalline solid, mp 112–114°C [Found: $(M + Na)^+$, 298.0416. $C_{11}H_{18}{}^{79}BrNO_2$ requires $(M + Na)^+$, 298.0419]. δ_H (300 MHz) 6.21 (td, *J* 4.0, 1.0, 1H), 4.70 (br d, *J* 7.0, 1H), 4.32 (br s, 1H), 2.14–2.02 (complex m, 2H), 1.96–1.79 (complex m, 2H), 1.74–1.54 (complex m, 2H), 1.46 (s, 9H). δ_C (75 MHz) 155.1 (C), 133.3 (CH), 122.9 (C), 79.5 (C), 51.7 (CH), 31.2 (CH_2), 28.3 (CH_3), 27.5 (CH_2), 17.9 (CH_2). ν_{max} 3255, 2978, 2947, 2912, 1702, 1676, 1541, 1364, 1266, 1249, 1170, 1056, 982 cm^{-1}. *m/z* (ESI, +ve) 300 and 298 [$(M + Na)^+$, both 100%].

*Compound **10***

Step i: A solution of carbamate **8** (1.61 g, 5.86 mmol) in dry CH_2Cl_2 (29 mL) was treated, dropwise over 10 min, with TFA (2.9 mL). The resulting mixture was stirred at 18°C under an atmosphere of nitrogen for 2.5 h and then NaOH (15 mL of a 2 M aqueous solution) was added. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic fractions were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford *amine **9*** (1.12 g, 88%) as a clear, yellow oil. This material was used directly in *Step ii* of the reaction sequence.

Step ii: A solution of amine **9** (1.12 g, 6.36 mmol) in dry CH_2Cl_2 (19 mL) was treated with *p*-toluenesulfonyl chloride (1.33 g, 7.00 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, single crystal) and dropwise over 10 min, triethylamine (1.06 mL, 7.93 mmol). The resulting mixture was stirred at 18°C for 1 h under an atmosphere of nitrogen. HCl (20 mL of a 2 M aqueous solution) was then added and the separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL) followed by ethyl acetate (2 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford a cream solid, recrystallization (CH_2Cl_2/hexane) of which afforded the *title compound **10*** (2.05 g, 98%) as white needles, mp 100–101°C, R_F 0.3 (in 3/7 v/v ethyl acetate/hexane) [Found: $(M + Na)^+$, 351.9987. $C_{13}H_{16}{}^{79}BrNO_2S$ requires $(M + Na)^+$, 351.9983]. δ_H (300 MHz) 7.80 (dm, *J* 8.4, 2H), 7.30 (dm, *J* 8.4, 2H), 6.19 (m, 1H), 4.80 (d, *J* 6.6, 1H), 3.81 (m, 1H), 2.42 (s, 3H), 2.15–1.93 (complex m, 3H), 1.81 (m, 1H), 1.66–1.57 (complex m, 2H). δ_C (75 MHz) 143.5 (C), 136.9 (C), 135.2 (CH), 129.5 (CH), 127.5 (CH), 120.1 (C), 55.1 (CH), 31.6 (CH_2), 27.4 (CH_2), 21.6 (CH_3), 16.5 (CH_2). ν_{max} 3276, 3063, 3041, 2942, 1642, 1598, 1446, 1427, 1330, 1156, 1087, 914, 813, 738, 665 cm^{-1}. *m/z* (ESI, +ve) 354 and 352 [$(M + Na)^+$, 92 and 88%], 102 (100).

*Compound **11***

A solution of amine **9** (1.62 g, 9.20 mmol) in dry CH_2Cl_2 (28 mL) was treated with triethylamine (1.54 mL, 11.04 mmol), DMAP (one crystal), and 2-nitrobenzenesulfonyl chloride (2.24 g, 10.12 mmol). The resulting mixture was stirred at 18°C under an atmosphere of nitrogen for 1.5 h and then treated with NH_4Cl (20 mL of a saturated aqueous solution). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic fractions were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.6 in 1/1 v/v ethyl acetate/hexane), the *title sulfonamide **11*** (3.31 mg, 99%) as a fine, white solid, mp 149–150°C [Found: $(M - H)^-$, 358.9697. $C_{12}H_{13}{}^{79}BrN_2O_4S$ requires $(M - H)^-$, 358.9701]. δ_H (300 MHz) 8.17 (m, 1H), 7.93 (m, 1H), 7.80–7.58 (complex m, 2H), 6.24 (m, 1H), 5.67 (d, *J* 7.1, 1H), 4.03 (m, 1H), 2.20–2.00 (complex m, 3H), 1.95–1.84 (m, 1H), 1.73–1.62 (complex m, 2H). δ_C (75 MHz) 147.5 (C), 135.7 (CH), 134.1 (C), 133.5 (CH), 132.9 (CH), 130.6 (CH), 125.4 (C), 119.3 (CH), 56.3 (CH), 32.2 (CH_2), 27.3 (CH_2), 16.3 (CH_2). ν_{max} 3351, 2939, 1539, 1410, 1358, 1172 cm^{-1}. *m/z* (ESI, –ve) 361 and 359 [$(M - H)^-$, 100 and 92%).

Compound ***12***

A solution of bromide **10** (580 mg, 1.76 mmol) in benzene (19 mL) and ethanol (1 mL) was treated with 3,4-methylenedioxyphenylboronic acid (320 mg, 1.93 mmol), tetrakis(triphenylphosphine)palladium(0) (101 mg, 0.09 mmol), and Na_2CO_3 (4.5 mL of a 2 M aqueous solution). The resulting mixture was stirred at 80°C under an atmosphere of nitrogen for 5 h and then $NaHCO_3$ (20 mL of a saturated aqueous solution) and ethyl acetate (20 mL) were added to the cooled reaction mixture. The separated aqueous phase was extracted with ethyl acetate (3×20 mL) and the combined organic fractions dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/4 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 3/7 v/v ethyl acetate/hexane), the *title compound* ***12*** (478 mg, 78%) as a white solid, mp 161.5–162.5°C [Found: $(M + Na)^+$, 394.1089. $C_{20}H_{21}NO_4S$ requires $(M + Na)^+$, 394.1089]. δ_H (300 MHz) 7.53 (dm, *J* 8.1, 2H), 7.18 (dm, *J* 8.1, 2H), 6.49 (dd, *J* 7.8, 0.3, 1H), 6.39 (dd, *J* 7.8 and 1.8, 1H), 6.33 (d, *J* 1.8, 1H), 5.94 (m, 1H), 5.90 (q, *J* 1.5, 2H), 4.41 (d, *J* 5.7, 1H), 4.09 (d, *J* 3.9, 1H), 2.42 (s, 3H), 2.23–2.02 (complex m, 3H), 1.74–1.61 (complex, 3H). δ_C (75 MHz) 147.2 (C), 146.5 (C), 142.9 (C), 137.0 (C), 135.8 (C), 133.7 (C), 130.3 (CH), 129.2 (CH), 126.9 (CH), 119.8 (CH), 107.8 (CH), 106.6 (CH), 100.8 (CH_2), 49.5 (CH), 29.9 (CH_2), 25.4 (CH_2), 21.4 (CH_3), 16.3 (CH_2). ν_{max} 3257, 2921, 1503, 1488, 1244, 1165, 1157, 1034, 929, 813, 798, 674 cm^{-1}. *m/z* (ESI, +ve) 394 [$(M + Na)^+$, 100%], 201 (73).

Compound ***13***

A solution of bromide **11** (188 mg, 0.52 mmol) and 3,4-methylenedioxyphenylboronic acid (146 mg, 0.88 mmol), triethylamine (1 mL), $PdCl_2(dppf)\cdot CH_2Cl_2$ (26 mg, 0.03 mmol), and water (0.2 mL) in THF (1.4 mL) was sparged with nitrogen for 5 min and then subjected to microwave irradiation at 90°C for 1.5 h. The cooled reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (2×20 mL) followed by brine (1×10 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 2/3 v/v ethyl acetate/hexane), the *title compound* ***13*** (160 mg, 77%) as a pale-yellow, crystalline solid, mp 158–165°C (Found: $M^{+\bullet}$, 402.0896. $C_{19}H_{18}N_2O_6S$ requires $M^{+\bullet}$, 402.0886). δ_H (300 MHz) 8.07 (dd, *J* 7.6 and 2.0, 1H), 7.74–7.62 (complex m, 3H), 6.44 (dd, *J* 7.6 and 2.4, 1H), 6.37 (s, 1H), 6.36 (d, *J* 6.8, 1H), 5.94 (m, 1H), 5.83 (s, 2H), 5.43 (d, *J* 6.8, 1H), 4.33 (m, 1H), 2.28–2.05 (complex m, 3H), 1.84–1.66 (complex m, 3H). δ_C (75 MHz) 147.0 (C), 146.8 (C), 146.5 (C), 136.0 (C), 134.4 (C), 134.0 (C), 132.9 (CH), 132.8 (CH), 131.0 (CH), 130.7 (CH), 125.5 (CH), 120.2 (CH), 107.7 (CH), 106.9 (CH), 100.8 (CH_2), 51.4 (CH), 30.9 (CH_2), 25.4 (CH_2), 16.3 (CH_2). ν_{max} 3354, 2934, 1537, 1488, 1440, 1402, 1358, 1341, 1244, 1171, 1039 cm^{-1}. *m/z* (EI) 402 ($M^{+\bullet}$, 62%), 200 (100).

Compound ***14***

A mixture of bromide **11** (200 mg, 0.55 mmol), methyl 6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzo[*d*][1,3]dioxole-5-carboxylate[5a] (275 mg, 0.94 mmol), triethylamine (1.1 mL), $PdCl_2(dppf)\cdot CH_2Cl_2$ (27 mg, 0.03 mmol), and water (0.3 mL) in THF (2.5 mL) was sparged with nitrogen for 5 min and then subjected to microwave irradiation at 90°C for 1.5 h. The cooled reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (2×20 mL) followed by brine (1×10 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_F 0.5 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***14*** (176 mg, 69%) as a white, foamy solid lacking a distinct melting point [Found: $(M + Na)^+$, 483.0825. $C_{21}H_{20}N_2O_8S$ requires $(M + Na)^+$, 483.0838]. δ_H (400 MHz) 7.86 (m, 1H), 7.61 (m, 1H), 7.58–7.55 (complex m, 2H), 6.98 (s, 1H), 6.49 (br s, 1H), 6.23 (s, 1H), 5.88 (d, *J* 1.2, 1H), 5.87 (d, *J* 1.2, 1H), 5.56 (m, 1H), 4.20 (m, 1H), 3.84 (s, 3H), 2.20–1.94 (complex m, 4H), 1.83–1.66 (complex m, 2H). δ_C (100 MHz) 167.3 (C), 149.4 (C), 146.8 (C), 146.3 (C), 138.4 (C), 136.6 (C), 134.4 (C), 132.4 (CH), 132.3 (CH), 130.4 (CH), 130.3 (CH), 124.7 (CH), 123.6 (C), 109.6 (CH), 109.4 (CH), 101.7 (CH_2), 53.9 (CH), 52.3 (CH_3), 31.9 (CH_2), 25.2 (CH_2), 17.9 (CH_2). ν_{max} 3315, 3095, 2950, 1710, 1614, 1540, 1486, 1375, 1250, 1172, 1216, 1037, 740 cm^{-1}. *m/z* (ESI, +ve) 483 [$(M + Na)^+$, 20%], 260 (25), 259 (100), 227 (36).

Compound ***15***

A solution of sulfonamide **12** (206 mg, 0.56 mmol) in dry DMF (3 mL), maintained at 0°C under an atmosphere of nitrogen, was treated with sodium hydride (60% dispersion in mineral oil, 27 mg, 0.67 mmol). After 1 h the reaction mixture was treated with propargyl bromide (310 μL of an 80% solution in toluene, 2.8 mmol) and then allowed to warm to 18°C, stirred at this temperature for 3.5 h, treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min, and then extracted with ethyl acetate (4×20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/9 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_F 0.5 in 3/7 v/v ethyl acetate/hexane) gave the *title compound* ***15*** (202 mg, 89%) as a pale-yellow solid, mp 144–146°C [Found: $(M + Na)^+$, 432.1250. $C_{23}H_{23}NO_4S$ requires $(M + Na)^+$, 432.1245]. δ_H (300 MHz) 7.73 (dt, *J* 8.4 and 1.8, 2H), 7.23 (dm, *J* 8.4, 2H), 6.71 (dd, *J* 7.5 and 1.8, 1H), 6.69 (s, 1H), 6.64 (dd, *J* 7.5 and 1.5, 1H), 6.11 (m, 1H), 5.92 (s, 2H), 5.03 (m, 1H), 3.93 (dd, *J* 18.6 and 2.4, 1H), 3.60 (dd, *J* 18.6 and 2.4, 1H), 2.42 (s, 3H), 2.21–2.10 (complex m, 2H), 2.07 (t, *J* 2.4, 1H), 2.04 (m, 1H), 1.92–1.75 (complex m, 2H), 1.61 (m, 1H). δ_C (75 MHz) 147.3 (C), 146.6 (C), 143.1 (C), 137.9 (C), 136.5 (C), 134.1 (CH), 133.2 (C), 129.2 (CH), 127.7 (CH), 120.1 (CH), 107.9 (CH), 107.3 (CH), 100.9 (CH_2), 80.2 (C), 72.3 (CH), 55.3 (CH), 33.3 (CH_2), 28.8 (CH_2), 25.5 (CH_2), 21.5 (CH_3), 20.2 (CH_2). ν_{max} 3290, 2937, 1597, 1503, 1489, 1438, 1334, 1244, 1155, 1038, 935, 807, 668 cm^{-1}. *m/z* (ESI, +ve) 432 [$(M + Na)^+$, 24%], 201 (100).

Compound ***16***

A magnetically stirred solution of sulfonamide **13** (119 mg, 0.30 mmol) in dry DMF (1.5 mL), maintained at 0°C under an atmosphere of argon, was treated with sodium hydride (60% dispersion in mineral oil, 14 mg, 0.36 mmol). After 1 h the reaction mixture was treated with propargyl bromide (33 μL of an 80% solution in toluene, 1.48 mmol) and then allowed to warm to 18°C and stirred at this temperature for 3 h. The reaction

mixture was then treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred at 18°C for 5 min, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution). Concentration of the relevant fractions (R_F 0.5 in 2/3 v/v ethyl acetate/hexane) gave the *title compound* ***16*** (118 mg, 91%) as a pale-yellow solid, mp 140–141°C [Found: $(M + Na)^+$, 463.0937. $C_{22}H_{20}N_2O_6S$ requires $(M + Na)^+$, 463.0940]. δ_H (400 MHz) 8.05 (dd, *J* 8.0 and 1.2, 1H), 7.67 (td, *J* 7.6 and 1.2, 1H), 7.61 (dd, *J* 8.0 and 1.6, 1H), 7.57 (td, *J* 7.6 and 1.6, 1H), 6.57 (dd, *J* 8.0 and 1.6, 1H), 6.54–6.51 (complex m, 2H), 6.09 (m, 1H), 5.88 (d, *J* 1.2, 1H), 5.87 (d, *J* 1.2, 1H), 4.99 (m, 1H), 4.11 (dd, *J* 18.4 and 2.4, 1H), 3.72 (dd, *J* 18.4 and 2.4, 1H), 2.28–2.08 (complex m, 4H), 2.17 (t, *J* 2.4, 1H), 1.86 (m, 1H), 1.70 (m, 1H). δ_C (100 MHz) 148.0 (C), 147.1 (C), 146.5 (C), 136.3 (C), 134.1 (CH), 133.5 (CH), 131.3 (CH), 131.2 (CH), 123.8 (CH), 120.2 (CH), 107.8 (CH), 107.3 (CH), 100.8 (CH_2), 80.2 (C), 72.7 (C), 56.2 (CH), 33.9 (CH_2), 29.3 (CH_2), 25.4 (CH_2), 20.2 (CH_2) (two signals obscured or overlapping). ν_{max} 3292, 3096, 2940, 2257, 1543, 1503, 1489, 1438, 1372, 1244, 1166, 1126, 1039, 935, 905, 736 cm^{-1}. *m/z* (ESI, +ve) 463 [$(M + Na)^+$, 100%], 201 (67).

Compound ***17***

A magnetically stirred solution of sulfonamide **14** (149 mg, 0.32 mmol) in dry DMF (1.6 mL), maintained at 0°C under an atmosphere of nitrogen, was treated with sodium hydride (60% dispersion in mineral oil, 16 mg, 0.39 mmol). After 1 h the reaction mixture was treated with propargyl bromide (180 μL of an 80% solution in toluene, 1.62 mmol) and then allowed to warm to 18°C, stirred at this temperature for 2 h, and then treated with NH_4Cl (20 mL of a saturated aqueous solution) and stirred for 5 min before being extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 2/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.3 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***17*** (128 mg, 80%) as a pale-yellow and foamy solid lacking a distinct melting point [Found: $(M + Na)^+$, 521.0998. $C_{24}H_{22}N_2O_8S$ requires $(M + Na)^+$, 521.0995]. δ_H (400 MHz) 7.90 (dd, *J* 8.2 and 1.4, 1H), 7.58 (td, *J* 7.6 and 1.2, 1H), 7.50–7.45 (complex m, 2H), 7.05 (s, 1H), 6.48 (s, 1H), 5.93 (d, *J* 1.2, 1H), 5.92 (d, *J* 1.2, 1H), 5.83 (td, *J* 3.8 and 1.6, 1H), 4.98 (m, 1H), 4.27 (dd, *J* 18.8 and 2.6, 1H), 4.01 (dd, *J* 18.8 and 2.0, 1H), 3.78 (s, 3H), 2.27–2.08 (complex m, 4H), 2.21 (t, *J* 2.4, 1H), 1.98–1.88 (complex m, 1H), 1.84–1.75 (complex m, 1H). δ_C (100 MHz) 166.1, 150.0, 147.3, 146.3, 138.4, 137.0, 133.3, 133.2, 133.1, 131.3, 131.2, 123.8, 122.0, 110.7, 110.0, 101.8, 80.5, 72.3, 56.7, 51.8, 34.2, 28.7, 25.1, 19.7. ν_{max} 3291, 2949, 1716, 1613, 1543, 1505, 1486, 1437, 1369, 1248, 1161, 1127, 1037, 874, 785, 738 cm^{-1}. *m/z* (ESI, +ve) 521 [$(M + Na)^+$, 19%), 259 (100).

Compound ***18***

A magnetically stirred solution of sulfonamide **13** (195 mg, 0.49 mmol) in dry DMF (2.4 mL), maintained at 0°C under an atmosphere of nitrogen, was treated with sodium hydride (60% dispersion in mineral oil, 23 mg, 0.58 mmol). After 1 h the mixture was treated with 1-bromobut-2-yne (322 μL, 2.42 mmol) and then allowed to warm to 18°C and stirred at this temperature for 2 h. After this time the reaction mixture was treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***18*** (189 mg, 86%) as a pale-yellow, crystalline solid, mp 159–163°C [Found: $(M + Na)^+$, 477.1095. $C_{23}H_{22}N_2O_6S$ requires $(M + Na)^+$, 477.1096]. δ_H (400 MHz) 8.04 (dd, *J* 8.0 and 1.6, 1H), 7.65 (td, *J* 7.6 and 1.6, 1H), 7.58 (dd, *J* 7.6 and 1.2, 1H), 7.54 (dd, *J* 7.6 and 1.6, 1H), 6.62 (dd, *J* 8.0 and 1.6, 1H), 6.59 (d, *J* 1.2, 1H), 6.56 (d, *J* 8.0, 1H), 6.08 (m, 1H), 5.88 (d, *J* 1.2, 1H), 5.87 (d, *J* 1.2, 1H), 5.01 (m, 1H), 4.03 (dq, *J* 18.4 and 2.4, 1H), 3.68 (dq, *J* 18.4 and 2.4, 1H), 2.26–2.05 (complex m, 4H), 1.92–1.83 (m, 1H), 1.75–1.66 (m, 1H), 1.66 (t, *J* 2.4, 3H). δ_C (100 MHz) 148.0 (C), 147.0 (C), 146.4 (C), 136.5 (C), 134.2 (C), 133.7 (C), 133.6 (CH), 133.2 (CH), 131.2 (CH), 130.8 (CH), 123.5 (CH), 120.2 (CH), 107.7 (CH), 107.4 (CH), 100.7 (CH_2), 80.5 (C), 75.3 (C), 56.0 (CH), 34.4 (CH_2), 29.2 (CH_2), 25.3 (CH_2), 20.1 (CH_2), 3.4 (CH_3). ν_{max} 3026, 2937, 1587, 1542, 1503, 1490, 1438, 1370, 1344, 1293, 1244, 1223, 1160, 1037, 933, 878, 808, 736 cm^{-1}. *m/z* (ESI, +ve) 477 [$(M + Na)^+$, 100%], 201 (50).

Compound ***19***

A magnetically stirred solution of sulfonamide **14** (78 mg, 0.19 mmol) in dry DMF (1 mL) maintained at 0°C under an atmosphere of nitrogen was treated with sodium hydride (10 mg of a 60% dispersion in mineral oil, 0.23 mmol). After 1 h the mixture was treated with 1-bromobut-2-yne (88 μL, 0.97 mmol) and then allowed to warm to 18°C and stirred at this temperature for 2 h. After this time the reaction mixture was treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/1 ethyl acetate/hexane), the *title compound* ***19*** (82 mg, 83%) as a pale-yellow, foamy solid lacking a distinct melting point [Found: $(M + Na)^+$, 535.1151. $C_{25}H_{24}N_2O_8S$ requires $(M + Na)^+$, 535.1151]. δ_H (400 MHz) 7.94 (d, *J* 8.0, 1H), 7.58 (m, 1H), 7.51–7.46 (complex m, 2H), 7.13 (s, 1H), 6.53 (s, 1H), 5.96 (d, *J* 1.2, 1H), 5.95 (d, *J* 1.2, 1H), 5.85 (m, 1H), 5.02 (m, 1H), 4.20 (dm, *J* 18.4, 1H), 3.94 (dm, *J* 18.4, 1H), 3.81 (s, 3H), 2.24–2.09 (complex m, 4H), 1.93 (m, 1H), 1.81 (m, 1H), 1.69 (t, *J* 2.4, 3H). δ_C (100 MHz) 166.2 (C), 150.0 (C), 147.6 (C), 146.3 (C), 138.6 (C), 137.5 (C), 133.7 (C), 132.9 (CH), 132.8 (CH), 131.3 (CH), 130.8 (CH), 123.6 (CH), 122.2 (C), 110.8 (CH), 110.0 (CH), 101.7 (CH_2), 80.2 (C), 75.5 (C), 56.7 (CH), 51.8 (CH_3), 34.7 (CH_2), 28.7 (CH_2), 25.1 (CH_2), 19.8 (CH_2), 3.4 (CH_3). ν_{max} 3094, 2949, 1718, 1613, 1543, 1505, 1485, 1437, 1369, 1248, 1161, 1127, 1036, 877, 785, 737 cm^{-1}. *m/z* (ESI, +ve) 535 [$(M + Na)^+$, 71%], 259 (100).

Compound ***21***

A magnetically stirred solution of ketone **20**[16] (4.90 g, 44.6 mmol) and 2,2-dimethylpropane-1,3-diol (13.93 g, 133.7 mmol) in dry THF (45 mL) was maintained at 0°C under

an atmosphere of nitrogen and treated, in three equal portions over 2 h, with boron trifluoride diethyl etherate (3.3 mL, 26.7 mmol). The resulting mixture was stirred at 0°C for a further 2.5 h and then poured into ice-cold $NaHCO_3$ (100 mL of a saturated aqueous solution). The separated aqueous layer was extracted with CH_2Cl_2 (6 × 50 mL) and then the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/49 v/v diethyl ether/pentane elution) to afford, after concentration of the relevant fractions (R_F in 0.6 in 1/4 v/v ethyl acetate/hexane), the *title compound* ***21*** (7.93 g, 91%) as a clear, colourless oil. δ_H (400 MHz) 5.83 (m, 2H), 5.12 (m, 2H), 5.09 (m, 2H), 3.53 (s, 4H), 2.51 (dt, *J* 7.6 and 0.8, 4H), 0.97 (s, 6H). δ_C (100 MHz) 132.9 (CH), 117.8 (CH_2), 99.2 (C), 70.2 (CH_2), 38.2 (CH_2), 29.8 (C), 22.6 (CH_3). ν_{max} 3077, 2955, 2865, 1642, 1473, 1434, 1395, 1330, 1173, 1150, 1097, 988, 912, 835 cm^{-1}. The volatility of this material precluded the acquisition of mass spectrometric data.

Compound ***22***

A magnetically stirred solution of diene **21** (2.00 g, 10.2 mmol) and the Grubbs' II catalyst (173 mg, 0.20 mmol) in dry CH_2Cl_2 (500 mL) was heated at 40°C for 3 h while being maintained under an atmosphere of nitrogen. The cooled reaction mixture was then concentrated under reduced pressure at −15°C and the ensuing residue subjected to flash chromatography (silica gel, 1/49 v/v diethyl ether/pentane elution). After concentration of the relevant fractions (R_F 0.5 in 1/4 v/v ethyl acetate/hexane) at −15°C, the *title compound* ***22*** (1.63 g, 95%) was obtained as a clear, colourless oil. δ_H (300 MHz) 5.67 (s, 2H), 3.52 (s, 4H), 2.66 (s, 4H), 0.99 (s, 6H). δ_C (75 MHz) 127.7 (CH), 109.2 (C), 71.9 (CH_2), 42.3 (CH_2), 30.0 (C), 22.4 (CH_3). *m*/*z* (EI, 70 eV) 168 ($M^{+\bullet}$, 27%), 32 (100). This rather volatile material was used immediately in the next step of the reaction sequence.

Compound ***23***

A mixture of cyclopentene **22** (1.53 g, 9.10 mmol), $CHBr_3$ (7.9 mL, 90.9 mmol), NaOH (7.3 g in 7.3 mL of water, 182 mmol), and TEBAC (42 mg, 0.18 mmol) in CH_2Cl_2 (8 mL), maintained at 18°C under an atmosphere of nitrogen, was stirred vigorously for 4 h and then diluted with CH_2Cl_2 (100 mL). The resulting slurry was filtered through a pad of Celite that was washed with CH_2Cl_2 (1 × 400 mL). The combined filtrates were concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/19 v/v diethyl ether/pentane elution) to afford, after concentration of the appropriate fractions (R_F 0.6 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***23*** (2.07 g, 67%) as a white, crystalline solid, mp 51–53°C [Found: $(M - Br\bullet)^+$, 259.0336. $C_{11}H_{16}{}^{79}Br_2O_2$ requires $(M - Br\bullet)^+$, 259.0334]. δ_H (500 MHz) 3.48 (s, 2H), 3.37 (s, 2H), 2.57 (m, 2H), 2.22 (m, 2H), 1.69 (d, *J* 15, 2H), 0.94 (s, 6H). δ_C (125 MHz) 115.2 (C), 73.2 (CH_2), 71.2 (CH_2), 44.9 (C), 38.2 (CH_2), 35.6 (CH), 29.9 (C), 22.3 (CH_3). ν_{max} 3055, 2963, 2935, 2859, 1468, 1423, 1242, 1114, 1036, 1014, 994, 850, 766, 730 cm^{-1}. *m*/*z* (EI) 261 and 259 [$(M - Br\bullet)^+$, 94 and 95%], 147 and 145 (71 and 69), 128 (100), 69 (95), 65 (80), 56 (54), 41 (70).

Compound ***24***

A magnetically stirred mixture of *gem*-dibromide **23** (1.28 g, 3.77 mmol) and silver cyanate (2.83 g, 18.87 mmol) in anhydrous 1,4-dioxane (19 mL) was heated at 80°C for 18 h while being maintained under an atmosphere of argon. After this time the reaction mixture was treated with *t*-butanol (1.9 mL) and then heated at 105°C for a further 24 h. The resulting slurry was cooled and then filtered through a pad of Celite that was washed with CH_2Cl_2 (200 mL) and the combined filtrates were then concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/9 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***24*** (1.04 g, 73%) as a white, crystalline solid, mp 86–90°C (Found: $M^{+\bullet}$, 375.1046. $C_{16}H_{26}{}^{79}BrNO_4$ requires $M^{+\bullet}$, 375.1045). δ_H (400 MHz) 6.00 (t, *J* 3.8, 1H), 5.09 (d, *J* 10.0, 1H), 4.49 (m, 1H), 3.56 (dd, *J* 11.2 and 8.0, 2H), 3.45 (t, *J* 10.0, 2H), 2.62 (dd, *J* 18.0 and 4.4, 1H), 2.35 (m, 1H), 2.24 (d, *J* 18.0, 1H), 2.16 (dd, *J* 14.4 and 5.6, 1H), 1.47 (s, 9H), 1.00 (s, 3H), 0.94 (s, 3H). δ_C (100 MHz) 155.4 (C), 127.9 (CH), 122.8 (C), 95.7 (C), 79.5 (C), 70.4 (CH_2), 70.3 (CH_2), 51.7 (CH), 36.4 (CH_2), 35.2 (CH_2), 30.0 (C), 28.4 (CH_3), 22.6 (CH_3), 22.5 (CH_3). ν_{max} 3444, 3348, 2957, 2869, 1713, 1493, 1366, 1244, 1166, 1114, 1051, 1018, 934, 733 cm^{-1}. *m*/*z* (EI, 70 eV) 377 and 375 ($M^{+\bullet}$, both 8%), 240 (83), 128 (100), 69 (67), 57 (82), 41 (55).

Compound ***25***

Step i: A magnetically stirred solution of carbamate **24** (284 mg, 0.76 mmol) and 2,6-lutidine (700 μL, 6.04 mmol) in dry CH_2Cl_2 (4 mL) was treated with TMSOTf (550 μL, 3.02 mmol) in a dropwise fashion over 10 min. The resulting mixture was stirred at 0°C under an atmosphere of nitrogen for 3 h and then quenched with NaOH (25 mL of a 2 M aqueous solution). The separated aqueous phase was extracted with ethyl acetate (3 × 30 mL) and the combined organic fractions were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford the *expected amine* as a clear, colourless oil. δ_H (300 MHz) 5.90 (t, *J* 4.5, 1H), 3.68 (d, *J* 11.7, 1H), 3.59 (d, *J* 11.7, 1H), 3.49–3.37 (complex m, 3H), 2.54–2.44 (complex m, 1H), 2.40–2.30 (complex m, 2H), 2.17 (ddd, *J* 13.5, 6.0, and 1.2, 1H), 1.71 (br s, 2H), 1.02 (s, 3H), 0.91 (s, 3H). This material was used, as obtained, in *Step ii* of the reaction sequence.

Step ii: A magnetically stirred solution of the amine obtained as described in *Step i* and triethylamine (315 μL, 2.26 mmol) in dry CH_2Cl_2 (4 mL) was treated with 2-nitrobenzenesulfonyl chloride (176 mg, 0.79 mmol) and the resulting mixture stirred at 18°C under an atmosphere of nitrogen for 2 h. NaOH (20 mL of a 2 M aqueous solution) was then added to the reaction mixture and the separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic fractions were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_F 0.4 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***25*** (252 mg, 72% from **24**) as a white, crystalline solid, mp 98–100°C (Found: $M^{+\bullet}$, 460.0309. $C_{17}H_{21}{}^{79}BrN_2O_6S$ requires $M^{+\bullet}$, 460.0304). δ_H (500 MHz) 8.19 (dd, *J* 8.0 and 1.8, 1H), 7.92 (dd, *J* 7.5 and 2.0, 1H), 7.76–7.68 (complex m, 2H), 6.46 (d, *J* 9.5, 1H), 6.03 (dd, *J* 5.0 and 3.0, 1H), 4.37 (m, 1H), 3.61 (dd, *J* 11.5 and 1.0, 1H), 3.52 (d, *J* 11.5, 1H), 3.48 (d, *J* 11.5, 1H), 3.44 (dd, *J* 11.5 and 1.0, 1H), 2.82 (ddd, *J* 18.0, 5.5, and 1.5, 1H), 2.25 (dt, *J* 14.0 and 2.5, 1H), 2.12 (ddd, *J* 18.0, 2.8, and 1.8, 1H), 2.05 (dd, *J* 14.0 and 5.5, 1H), 0.91 (s, 3H), 0.89 (s, 3H). δ_C (125 MHz) 147.5 (C), 135.5 (C), 133.3 (CH), 133.0 (CH), 130.4 (CH),

129.6 (CH), 125.4 (CH), 120.5 (C), 95.2 (C), 70.4 (2 × CH_2), 56.4 (CH), 37.4 (CH_2), 34.4 (CH_2), 30.0 (C), 22.3(1) (CH_3), 22.2(6) (CH_3). ν_{max} 3307, 2957, 2869, 1541, 1412, 1352, 1173, 1155, 1126, 1087, 911, 733 cm^{-1}. *m*/*z* (EI) 462 and 460 ($M^{+\bullet}$, both 34%), 274 and 272 (both 87), 261 and 259 (both 53), 186 (70), 128 (100), 69 (85), 41 (78).

Compound ***26***

A mixture of bromide **25** (300 mg, 0.65 mmol) and 3,4-methylenedioxyphenyl boronic acid (183 mg, 1.11 mmol), triethylamine (1.3 mL), $PdCl_2(dppf)\cdot CH_2Cl_2$ (32 mg, 0.04 mmol), and water (0.3 mL) in THF (2.7 mL) was sparged with nitrogen for 5 min and then subjected to microwave irradiation at 90°C for 1.5 h. The cooled reaction mixture was diluted with ethyl acetate (20 mL) and then washed with water (2 × 20 mL) and brine (10 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***26*** (284 mg, 81%) as a pale-yellow and foamy solid lacking a distinct melting point (Found: $M^{+\bullet}$, 502.1411. $C_{24}H_{26}N_2O_8S$ requires $M^{+\bullet}$, 502.1410). δ_H (400 MHz) 7.90 (m, 1H), 7.80 (m, 1H), 7.63–7.57 (complex m, 2H), 6.68 (dd, *J* 8.4 and 2.0, 1H), 6.60 (d, *J* 1.2, 1H), 6.52 (d, *J* 8.4, 1H), 6.34 (d, *J* 9.2, 1H, NH), 5.88 (s, 2H), 5.75 (m, 1H), 4.76 (br m, 1H), 3.67 (d, *J* 12.0, 1H), 3.56 (d, *J* 12.0, 1H), 3.52 (s, 2H), 2.88 (ddd, *J* 18.8, 5.2, and 2.0, 1H), 2.48 (dt, *J* 14.0 and 2.2, 1H), 2.25 (ddd, *J* 18.8, 2.8, and 2.0, 1H), 1.96 (dd, *J* 14.0 and 4.8, 1H), 0.97 (s, 3H), 0.88 (s, 3H). δ_C (100 MHz) 147.2 (C), 146.8 (C), 136.2 (C), 135.8 (C), 133.2 (C), 132.8 (CH), 132.5 (CH), 129.9 (CH), 125.2 (CH), 124.8 (CH), 120.3 (CH), 107.9 (CH), 107.2 (CH), 100.9 (CH_2), 96.1 (C), 70.4 (CH_2), 70.3 (CH_2), 51.8 (CH), 35.7 (CH_2), 33.7 (CH_2), 30.0 (C), 22.4 (CH_3), 22.3 (CH_3) (one signal obscured or overlapping). ν_{max} 3307, 2957, 2870, 1594, 1540, 1490, 1440, 1409, 1344, 1243, 1170, 1123, 1038, 934, 733 cm^{-1}. *m*/*z* (EI, 70 eV) 502 ($M^{+\bullet}$, 16%), 374 (98), 316 (25), 214 (24), 188 (100), 158 (35), 129 (48), 69 (38).

Compound ***27***

A solution of bromide **25** (378 mg, 0.82 mmol) in THF (4.1 mL) was treated with methyl 6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzo[*d*][1,3]dioxole-5-carboxylate[5a] (263 mg, 0.901 mmol), Cs_2CO_3 (801 mg, 2.46 mmol), potassium acetate (81 mg, 0.82 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (33 mg, 0.04 mmol), and water (0.41 mL). The ensuing mixture was sparged with nitrogen and then heated at 65°C for 2 h, cooled, diluted with ethyl acetate (40 mL) and then washed with water (1 × 40 mL) and brine (1 × 40 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***27*** (310 mg, 68%) as a colourless, crystalline solid, mp 176–179°C (Found: $M^{+\bullet}$, 560.1463. $C_{26}H_{28}N_2O_{10}S$ requires $M^{+\bullet}$, 560.1465). δ_H (500 MHz) 7.77 (dd, *J* 7.0 and 1.0, 1H), 7.70 (dd, *J* 7.5 and 1.5, 1H), 7.59–7.51 (complex m, 2H), 7.12 (s, 1H), 5.58 (d, *J* 8.5, 1H), 6.34 (s, 1H), 5.89 (m, 2H), 5.37 (t, *J* 3.5, 1H), 4.53 (m, 1H), 3.84 (s, 3H), 3.75 (d, *J* 11.0, 1H), 3.67 (d, *J* 12.0, 1H), 3.55–3.48 (complex m, 2H), 2.64 (d, *J* 17.5, 1H), 2.44 (m, 1H), 2.37–2.32 (complex m, 2H), 1.06 (s, 3H), 0.90 (s, 3H). δ_C (125 MHz) 166.9, 149.7, 146.9, 146.6, 138.0, 137.9, 135.4, 132.6, 132.1, 129.8, 124.8, 124.3, 110.7, 109.7, 101.7, 96.6, 70.4(3), 70.3(8), 54.1, 52.3, 35.4, 35.3, 30.1, 22.7, 22.3 (one signal obscured or overlapping). ν_{max} 3307, 2955, 2870, 1711, 1613, 1540, 1505, 1486, 1437, 1407, 1370, 1344, 1252, 1168, 1123, 1038, 910, 731 cm^{-1}. *m*/*z* (EI, 70 eV) 560 ($M^{+\bullet}$, 13%), 432 (74), 374 (77), 214 (100), 129 (50), 128 (46), 69 (51).

Compound ***28***

A magnetically stirred solution of sulfonamide **26** (130 mg, 0.26 mmol) in dry DMF (1.3 mL), maintained at 0°C under an atmosphere of nitrogen, was treated with sodium hydride (13 mg of a 60% dispersion in mineral oil, 0.31 mmol). After 1 h the reaction mixture was treated with propargyl bromide (145 μL of an 80% solution in toluene, 1.29 mmol) and then allowed to warm to 18°C and stirred at this temperature for 2 h. The reaction mixture was then treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min at 18°C, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/4 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.6 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***28*** (124 mg, 89%) as a white, crystalline solid, mp 159–161°C [Found: $(M + Na)^+$, 563.1464. $C_{27}H_{28}N_2O_8S$ requires $(M + Na)^+$, 563.1464]. δ_H (400 MHz) 8.05 (d, *J* 8.0, 1H), 7.73–7.61 (complex m, 3H), 6.50–6.49 (complex m, 2H), 6.36 (m, 1H), 5.86 (d, *J* 1.4, 1H), 5.85 (m, 1H), 5.84 (d, *J* 1.4, 1H), 5.06 (m, 1H), 4.08 (dd, *J* 18.8 and 2.4, 1H), 3.79 (d, *J* 11.2, 1H), 3.71 (d, *J* 11.2, 1H), 3.66 (dd, *J* 18.8 and 2.4, 1H), 3.51 (dd, *J* 18.8 and 1.6, 1H), 3.48 (dd, *J* 18.8 and 1.6, 1H), 3.06 (ddd, *J* 13.6, 6.0, and 2.8, 1H), 2.66 (m, 1H), 2.41 (dt, *J* 18.0 and 3.6, 1H), 2.35 (dd, *J* 13.2 and 10.0, 1H), 2.17 (t, *J* 2.4, 1H), 1.09 (s, 3H), 0.93 (s, 3H). δ_C (100 MHz) 147.9 (C), 147.0 (C), 146.6 (C), 136.5 (C), 133.7 (CH), 133.3 (C), 133.2 (C), 131.4 (CH), 131.2 (CH), 128.7 (CH), 124.1 (CH), 120.2 (CH), 107.7 (CH), 107.3 (CH), 100.8 (CH_2), 97.0 (C), 80.0 (C), 73.0 (C), 70.4(3) (CH_2), 70.3(8) (CH_2), 57.0 (CH), 36.1 (CH_2), 34.0 (CH_2), 32.8 (CH_2), 30.1 (CH), 22.7 (CH_3), 22.3 (CH_3). ν_{max} 3292, 2956, 2870, 2122, 1544, 1489, 1371, 1351, 1246, 1167, 1117, 1084, 1038, 935, 892, 737 cm^{-1}. *m*/*z* (ESI, +ve) 563 $[(M + Na)^+$, 19%], 302 (20), 301 (100).

Compound ***29***

A magnetically stirred solution of sulfonamide **27** (95 mg, 0.170 mmol) in dry DMF (1 mL) maintained at 0°C under an atmosphere of nitrogen was treated with sodium hydride (8 mg of a 60% dispersion in mineral oil, 0.20 mmol). After 1.5 h the mixture was treated with propargyl bromide (60 μL of an 80% solution in toluene, 0.84 mmol), allowed to warm to 18°C, and then stirred at this temperature for 2 h. The reaction mixture was then treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min at 18°C, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.3 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***29*** (75 mg, 74%) as a pale-yellow and foamy solid lacking a distinct melting point [Found: $(M + Na)^+$, 621.1511. $C_{29}H_{30}N_2O_{10}S$ requires $(M + Na)^+$, 621.1519]. δ_H (400 MHz) 7.99 (d, *J* 7.6, 1H), 7.65

(m, 1H), 7.59–7.55 (complex m, 2H), 7.15 (s, 1H), 6.41 (br s, 1H), 5.94 (m, 2H), 5.62 (m, 1H), 5.20 (br s, 1H), 4.20–4.00 (complex m, 2H), 3.83 (d, *J* 11.6, 1H), 3.78 (s, 3H), 3.74 (d, *J* 11.6, 1H), 3.56 (dd, *J* 11.6 and 1.2, 1H), 3.47 (dd, *J* 11.6 and 1.2, 1H), 3.08 (ddd, *J* 13.6, 5.2, and 2.4, 1H), 2.62 (dm, *J* 18.0, 1H), 2.40 (dt, *J* 18.0 and 2.8, 1H), 2.23 (dd, *J* 13.2 and 2.8, 1H), 2.15 (t, *J* 2.4, 1H), 1.11 (s, 3H), 0.91 (s, 3H). δ_C (100 MHz) 166.6, 149.9, 147.7, 146.6, 136.7, 133.5, 131.7, 131.4, 128.8, 124.1, 123.1, 110.2, 101.8, 97.2, 80.4, 72.8, 70.5, 70.4, 58.0, 52.0, 36.6, 34.4, 32.3, 30.2, 22.9, 22.4 (signals attributable to three carbons obscured or overlapping). ν_{max} 3290, 2954, 2870, 2251, 1718, 1544, 1505, 1486, 1436, 1367, 1252, 1167, 1126, 1036, 910, 885, 732 cm^{-1}. *m/z* (ESI, +ve) 621 [$(M + Na)^+$, 46%], 359 (100).

*Compound **30***

A magnetically stirred solution of sulfonamide **26** (100 mg, 0.20 mmol) in dry DMF (1 mL), maintained at 0°C under an atmosphere of nitrogen, was treated with sodium hydride (10 mg of a 60% dispersion in mineral oil, 0.24 mmol). After 2 h at 0°C the reaction mixture was treated with 1-bromobut-2-yne (90 μL, 1.0 mmol), allowed to warm to 18°C, and then maintained at this temperature for 2 h. After this time the reaction mixture was treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min at 18°C, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.6 in 1/1 v/v ethyl acetate/hexane), the *title compound **30*** (94 mg, 85%) as a clear, colourless oil [Found: $(M + Na)^+$, 577.1616. $C_{28}H_{30}N_2O_8S$ requires $(M + Na)^+$, 577.1621]. δ_H (400 MHz) 8.02 (d, *J* 7.6, 1H), 7.68 (m, 1H), 7.63–7.57 (complex m, 2H), 6.55 (dd, *J* 8.0 and 1.6, 1H), 6.49 (d, *J* 8.0, 1H), 6.45 (d, *J* 1.6, 1H), 5.86 (d, *J* 1.4, 1H), 5.84 (d, *J* 1.4, 1H), 5.83 (m, 1H), 5.08 (m, 1H), 3.98 (dq, *J* 18.4 and 2.4, 1H), 3.79 (d, *J* 11.6, 1H), 3.70 (d, *J* 11.6, 1H), 3.63 (dq, *J* 18.4, 1H), 3.50 (dd, *J* 17.3 and 1.6, 1H), 3.47 (dd, *J* 17.3 and 1.6, 1H), 3.00 (ddd, *J* 13.5, 5.9, and 2.7, 1H), 2.65 (m, 1H), 2.39 (dm, *J* 17.9, 1H), 2.29 (dd, *J* 13.5 and 10.4, 1H), 1.63 (t, *J* 2.3, 3H), 1.08 (s, 3H), 0.92 (s, 3H). δ_C (100 MHz) 148.0 (C), 147.0 (C), 146.6 (C), 136.9 (C), 133.7 (C), 133.5 (C), 133.3 (CH), 131.3 (CH), 131.1 (CH), 128.3 (CH), 123.9 (CH), 120.4 (CH), 107.7 (CH), 107.5 (CH), 100.8 (CH_2), 97.1 (C), 80.8 (C), 75.0 (C), 70.5 (CH_2), 70.4 (CH_2), 56.9 (CH), 36.1 (CH_2), 34.6 (CH_2), 32.7 (CH_2), 30.2 (C), 22.8 (CH_3), 22.3 (CH_3), 3.5 (CH_3). ν_{max} 2956, 2870, 2249, 1544, 1489, 1372, 1349, 1246, 1166, 1114, 1038, 908, 735 cm^{-1}. *m/z* (ESI, +ve) 577 [$(M + Na)^+$, 18%], 301 (100).

*Compound **31***

A magnetically stirred solution of sulfonamide **27** (170 mg, 0.303 mmol) in dry DMF (1.5 mL) maintained at 0°C under an atmosphere of nitrogen was treated with sodium hydride (15 mg of a 60% dispersion in mineral oil, 0.36 mmol). After 1 h the mixture was treated with 1-bromobut-2-yne (137 μL, 1.52 mmol), allowed to warm to 18°C, and then stirred at this temperature for 2 h. After this time the reaction mixture was treated with NH_4Cl (20 mL of a saturated aqueous solution), stirred for 5 min at 18°C, and then extracted with ethyl acetate (4 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/1 v/v ethyl acetate/hexane), the *title compound **31*** (178 mg, 96%) as a pale-yellow and foamy solid lacking a distinct melting point [Found: $(M + Na)^+$, 635.1683. $C_{30}H_{32}N_2O_{10}S$ requires $(M + Na)^+$, 635.1675]. δ_H (400 MHz) 7.97 (d, *J* 7.6, 1H), 7.63 (m, 1H), 7.58–7.52 (complex m, 2H), 7.21 (s, 1H), 6.51 (s, 1H), 5.96 (d, *J* 1.2, 1H), 5.95 (d, *J* 1.2, 1H), 5.63 (m, 1H), 5.22 (m, 1H), 4.10–3.92 (complex m, 2H), 3.87 (d, *J* 11.6, 1H), 3.79 (s, 3H), 3.74 (d, *J* 11.2, 1H), 3.57 (dd, *J* 11.6 and 1.6, 1H), 3.47 (dd, *J* 11.2 and 1.6, 1H), 3.03 (ddd, *J* 13.6, 5.6, and 2.4, 1H), 2.63 (m, 1H), 2.39 (m, 1H), 2.17 (dd, *J* 13.6 and 11.0, 1H), 1.62 (t, *J* 2.4, 3H), 1.12 (s, 3H), 0.92 (s, 3H). δ_C (100 MHz) 166.6 (C), 149.9 (C), 147.8 (C), 146.6 (C), 136.8 (C), 133.8 (C), 133.2 (CH), 131.5 (CH), 131.0 (CH), 128.3 (CH), 123.8 (CH), 123.2 (C), 110.5 (CH), 110.1 (CH), 101.7 (CH_2), 97.1 (C), 80.6 (C), 75.2 (C), 70.4 (CH_2), 70.3 (CH_2), 57.9 (CH), 51.9 (CH_3), 36.4 (CH_2), 34.8 (C), 32.2 (CH_2), 30.1 (CH_2), 29.6 (C), 22.9 (CH_3), 22.3 (CH_3), 3.4 (CH_3). ν_{max} 2953, 2925, 2869, 1719, 1544, 1486, 1366, 1253, 1166, 1125, 1036, 887, 737 cm^{-1}. *m/z* (ESI, +ve) 635 [$(M + Na)^+$, 100%], 359 (48).

*Compounds **32** and **37***

A magnetically stirred mixture of enyne **15** (200 mg, 0.49 mmol), $Pd(OAc)_2$ (5.5 mg, 0.024 mmol), and BBEDA (6.4 mg, 0.027 mmol) in dry 1,2-dichloroethane (24 mL) was heated at 56°C under an atmosphere of argon for 2 h. The solvent was then removed under reduced pressure and the residue thus obtained was subjected to flash chromatography (silica gel, 1/9 v/v ethyl acetate/hexane elution) thereby affording two fractions, A and B.

Concentration of fraction A (R_F 0.2 in 1/1 v/v ethyl acetate/hexane) gave an amorphous white solid (102 mg) that was tentatively assigned as a ~1:1 mixture of the two diastereoisomeric forms of the *title compound **32*** (60%).

Concentration of fraction B (R_F 0.5 in 1/1 v/v ethyl acetate/hexane) gave the *title compound **37*** (54 mg, 26%) as colourless crystals, mp 202–214°C (dec.) [Found: $(M + H)^+$, 410.1425. $C_{23}H_{23}NO_4S$ requires $(M + H)^+$, 410.1426]. δ_H (300 MHz) 7.51 (dm, *J* 8.2, 2H), 7.16 (dm, *J* 8.2, 2H), 6.52 (dd, *J* 8.1 and 0.4, 1H), 6.46 (dd, *J* 8.1 and 1.8, 1H), 6.33 (d, *J* 1.8, 1H), 5.94–5.86 (complex m, 3H), 5.44 (dt, *J* 10.0 and 1.9, 1H), 5.15 (t, *J* 1.9, 1H), 4.82 (t, *J* 2.2, 1H), 4.19 (dt, *J* 14.3 and 1.9, 1H), 3.97 (dt, *J* 14.3 and 1.9, 1H), 3.77 (dd, *J* 8.2 and 3.5, 1H), 2.41 (s, 3H), 2.36–2.24 (complex m, 1H), 2.20–2.06 (complex m, 1H), 2.02–1.89 (complex m, 1H), 1.88–1.78 (complex m, 1H). δ_C (75 MHz) 149.7, 147.3, 146.2, 143.2, 137.4, 133.9, 129.8, 129.3, 127.6, 127.3, 121.2, 110.4, 108.2, 107.6, 101.0, 67.5, 55.5, 52.6, 26.0, 21.8, 21.5. ν_{max} 2923, 1504, 1484, 1343, 1238, 1161, 1097, 1040, 934, 812, 664 cm^{-1}. *m/z* (ESI, +ve) 432 [$(M + Na)^+$, 100%], 410 [$(M + H)^+$, 9], 239 (45).

*Compounds **33** and **38***

A magnetically stirred mixture of enyne **16** (100 mg, 0.23 mmol), $Pd(OAc)_2$ (2.6 mg, 0.01 mmol), and BBEDA (3.0 mg, 0.013 mmol) in dry 1,2-dichloroethane (5 mL) was heated at 56°C under an atmosphere of argon for 4 h. The cooled reaction mixture was concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford two fractions, A and B.

Concentration of fraction A (R_F 0.3 in 2/3 v/v ethyl acetate/hexane) gave *dimer **33*** (66 mg, 66%) as a white, powdery solid, mp >240°C [Found: $(M+Na)^+$, 903.1980. $C_{44}H_{40}N_4O_{12}S_2$ requires $(M+Na)^+$, 903.1982]. δ_H (400 MHz) 8.02 (dt, *J* 7.6 and 2.0, 1H), 7.91 (dm, *J* 8.0, 1H), 7.70–7.51 (complex m, 6H), 6.68–6.55 (complex m, 3H), 6.43–6.34 (complex m, 2H), 6.28 (dd, *J* 6.8 and 1.6, 1H), 6.11 (m, 1H), 6.00 (m, 1H), 5.88 (s, 2H), 5.84 (m, 2H), 5.45 (s, 1H), 5.27 (d, *J* 2.4, 1H), 5.06 (m, 1H), 4.80 (m, 1H), 4.18 (d, *J* 18.0, 1H), 3.86 (m, 2H), 3.59 (t, *J* 18.0, 1H), 2.30–2.06 (complex m, 8H), 1.87 (m, 1H), 1.76–1.59 (complex m, 3H). δ_C (100 MHz) 148.1, 147.8, 147.2, 146.9, 146.6, 146.4, 136.6, 136.5, 135.9(9), 135.9(6), 134.9, 134.8(1), 134.7(6), 134.2(2), 134.1(9), 134.0, 133.9, 133.6, 133.5, 133.4(1), 133.3(6), 131.5, 131.3, 131.2, 131.1, 128.5(3), 128.4(9), 124.1 (1), 124.0(7), 123.7(3), 123.6(7), 123.2, 123.1, 120.3, 107.8, 107.7(3), 107.6(9), 107.4(5), 107.4(2), 107.3(5), 100.8(4), 100.7(7), 87.7, 82.9, 60.4, 56.2, 55.8(8), 55.8(3), 49.9, 34.7, 22.6, 30.5(3), 30.4(7), 29.3(4), 29.3(0), 25.5, 25.4, 22.6, 21.0, 20.3(4), 20.2(8), 19.5, 14.2. ν_{max} 2938, 2906, 1543, 1503, 1488, 1438, 1371, 1351, 1244, 1222, 1162, 1125, 1038, 935, 872, 807, 737 cm^{-1}. *m/z* (ESI, +ve) 919 [$(M+K)^+$, 100%], 903 [$(M+Na)^+$, 86].

Concentration of fraction B (R_F 0.6 in 2/3 v/v ethyl acetate/hexane) gave the *title compound **38*** (26 mg, 26%) as a white, crystalline solid, mp 159–160°C [Found: $(M+Na)^+$, 463.0940. $C_{22}H_{20}N_2O_6S$ requires $(M+Na)^+$, 463.0940]. δ_H (400 MHz) 7.61 (dd, *J* 8.0 and 1.6, 1H), 7.56 (td, *J* 7.6 and 1.2, 1H), 7.47–7.37 (complex m, 2H), 6.63 (dd, *J* 7.6 and 1.6, 1H), 6.58 (d, *J* 1.6, 1H), 6.49 (d, *J* 7.6, 1H), 5.88 (d, *J* 1.2, 1H), 5.86 (d, *J* 1.2, 1H), 5.85 (m, 1H), 5.55 (dt, *J* 9.6 and 2.0, 1H), 5.33 (t, *J* 1.8, 1H), 5.03 (t, *J* 2.2, 1H), 4.41 (dt, *J* 14.4 and 2.2, 1H), 4.24 (dt, *J* 14.8 and 1.8, 1H), 4.19 (dd, *J* 10.4 and 3.8, 1H), 2.25–2.17 (complex m, 2H), 1.99 (m, 1H), 1.81 (m, 1H). δ_C (100 MHz) 149.0 (C), 148.1 (C), 147.4 (C), 146.3 (C), 137.3 (C), 132.8 (CH), 131.8 (C), 131.0 (CH), 129.9 (CH), 129.8 (CH), 127.1 (CH), 123.5 (CH), 120.8 (CH), 111.3 (CH), 108.1 (CH), 107.7 (CH), 101.0 (CH_2), 67.3 (CH_2), 55.7 (C), 52.0 (CH_2), 26.7 (CH_2), 22.9 (CH_2). ν_{max} 2916, 1542, 1504, 1485, 1355, 1242, 1169, 1127, 1091, 1038, 934 cm^{-1}. *m/z* (ESI, +ve) 463 [$(M+Na)^+$, 100%], 441 [$(M+H)^+$, 30], 239 (65).

*Compound **34***

A mixture of enyne **17** (30 mg, 0.06 mmol), $Pd(OAc)_2$ (0.7 mg, 0.003 mmol), and Ph_3P (1.6 mg, 0.006 mmol) in dry benzene (5 mL) was heated at 80°C under an atmosphere of argon for 1 h. The reaction mixture was then cooled and concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica gel, 1/3 → 2/3 v/v ethyl acetate/hexane gradient elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 1/3 v/v ethyl acetate/hexane), *dimer **34*** (14 mg, 47%) as a white, powdery solid, mp >240°C [Found: $(M+Na)^+$, 1019.2099. $C_{48}H_{44}N_4O_{16}S_2$ requires $(M+Na)^+$, 1019.2091]. δ_H (400 MHz) 7.94 (dd, *J* 7.6 and 2.0, 1H), 7.78 (m, 1H), 7.64–7.48 (complex m, 4H), 7.47–7.41 (complex m, 2H), 7.19 (d, *J* 2.5, 1H), 6.96 (d, *J* 2.5, 1H), 6.60 (d, *J* 3.2, 1H), 6.55 (s, 0.5H), 6.48 (s, 0.5H), 6.00–5.96 (complex m, 3H), 5.03 (m, 1H), 5.89 (m, 1H), 5.81 (m, 1H), 5.59 (m, 1H), 5.32 (d, *J* 16.0, 1H), 5.12 (m, 1H), 4.93 (m, 1H), 4.35 (dd, *J* 16.0 and 3.2, 1H), 4.20–4.00 (complex m, 3H), 3.84 (s, 3/2H), 3.83 (s, 3/2H), 3.79 (s, 3/2H), 3.78 (s, 3/2H), 2.35–2.05 (complex m, 8H), 1.90 (m, 1H), 1.85 (m, 1H), 1.68 (m, 2H). *m/z* (ESI, +ve) 1035 [$(M+K)^+$, 5%], 1019 [$(M+Na)^+$, 100].

*Compound **35***

A mixture of enyne **28** (53 mg, 0.1 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), and Ph_3P (3.0 mg, 0.01 mmol) in dry benzene (9.8 mL) was heated at 80°C under an atmosphere of argon for 2 h. The reaction mixture was then cooled and concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica gel, 1/4 → 7/14 v/v ethyl acetate/hexane gradient elution) to afford, after concentration of the relevant fractions (R_F 0.3 in 1/1 v/v ethyl acetate/hexane) a powdery white solid (28 mg) that was tentatively assigned as a ~1:1 mixture of the two diastereoisomeric forms of the *title compound **35*** (53%).

*Compound **36***

A mixture of enyne **29** (29 mg, 0.05 mmol), $Pd(OAc)_2$ (0.5 mg, 0.002 mmol), and Ph_3P (1.27 mg, 0.005 mmol) in dry benzene (5 mL) was heated at 80°C under an atmosphere of argon for 2 h. The reaction mixture was then cooled and concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica gel, 3/7 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.3), a powdery white solid (21 mg) that was tentatively assigned as a ~1:1 mixture of the two diastereoisomeric forms of the *title compound **36*** (72%).

*Compound **39***

A magnetically stirred mixture of enyne **18** (50 mg, 0.11 mmol), $Pd(OAc)_2$ (7.4 mg, 0.033 mmol), and BBEDA (7.8 mg, 0.033 mmol) in dry benzene (5.5 mL) was heated at 80°C under an atmosphere of argon for 7 h. The reaction mixture was then cooled and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 1/1 v/v ethyl acetate/hexane), the *title compound **39*** (47 mg, 94%) as colourless crystals, mp 156–161°C [Found: $(M+Na)^+$, 477.1096. $C_{23}H_{22}N_2O_6S$ requires $(M+Na)^+$, 477.1096]. δ_H (400 MHz) 7.58 (dd, *J* 8.4 and 1.2, 1H), 7.53 (dd, *J* 8.4 and 1.6, 1H), 7.45–7.35 (complex m, 2H), 6.58 (dd, *J* 8.0 and 2.0, 1H), 6.54 (d, *J* 2.0, 1H), 6.46 (d, *J* 8.0, 1H), 5.87 (d, *J* 1.2, 1H), 5.85 (d, *J* 1.2, 1H), 5.82 (m, 1H), 5.54 (dt, *J* 8.0 and 2.0, 1H), 5.38 (m, 1H), 4.33 (m, 1H), 4.28 (m, 1H), 4.12 (dd, *J* 10.6 and 3.8, 1H), 2.21–2.17 (complex m, 2H), 1.98 (m, 1H), 1.78 (m, 1H), 1.73 (d, *J* 6.8, 3H). δ_C (100 MHz) 148.0 (C), 147.2 (C), 146.1 (C), 140.5 (C), 138.5 (C), 132.7 (CH), 132.0 (C), 131.0 (CH), 130.3 (CH), 129.9 (CH), 126.4 (CH), 123.4 (CH), 121.4 (CH), 120.9 (CH), 108.1 (CH), 107.6 (CH), 100.9 (CH_2), 67.5 (CH), 55.4 (C), 49.1 (CH_2), 26.6 (CH_2), 23.1 (CH_2), 14.6 (CH_3). ν_{max} 3025, 2918, 1543, 1504, 1484, 1435, 1372, 1354, 1239, 1166, 1127, 1039, 911, 729, 605 cm^{-1}. *m/z* (ESI, +ve) 477 [$(M+Na)^+$, 100%], 455 [$(M+H)^+$, 12], 253 (18).

*Compound **40***

A magnetically stirred mixture of enyne **30** (27 mg, 0.05 mmol), $Pd(OAc)_2$ (3.3 mg, 0.015 mmol), and BBEDA (3.5 mg, 0.015 mmol) in dry benzene (2.4 mL) was heated at 80°C under an atmosphere of argon for 5 h. The cooled reaction mixture was then concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_F 0.6 in 1/1 v/v ethyl acetate/hexane), the *title compound **40*** (27 mg, quantitative) as a

colourless solid lacking a defined melting point [Found: $(M+Na)^+$, 577.1620. $C_{28}H_{30}N_2O_8S$ requires $(M+Na)^+$, 577.1621]. δ_H (400 MHz) 7.48 (td, *J* 8.0 and 1.2, 1H), 7.44 (dd, *J* 8.0 and 1.2, 1H), 7.37 (dd, *J* 8.0 and 1.2, 1H), 7.27 (m, 1H), 6.56 (dd, *J* 6.4 and 2.0, 1H), 6.55 (s, 1H), 6.40 (m, 1H), 5.94 (dd, *J* 10.0 and 1.6, 1H), 5.85 (d, *J* 1.4, 1H), 5.84 (d, *J* 1.4, 1H), 5.72 (d, *J* 10.0, 1H), 5.50 (m, 1H), 4.47 (dd, *J* 12.4 and 4.4, 1H), 4.35 (br s, 2H), 3.77 (d, *J* 11.6, 1H), 3.68 (d, *J* 11.2, 1H), 3.62 (dd, *J* 11.6 and 1.2, 1H), 3.55 (dd, *J* 11.2 and 1.2, 1H), 2.93 (ddd, *J* 12.8, 4.4, and 1.6, 1H), 1.77 (d, *J* 6.8, 3H), 1.67 (t, *J* 12.4, 1H), 1.11 (s, 3H), 0.95 (s, 3H). δ_C (100 MHz) 147.8 (C), 147.3 (C), 146.3 (C), 134.1 (C), 137.8 (C), 133.2 (CH), 132.5 (CH), 131.8 (C), 130.9 (CH), 129.6 (CH), 126.3 (CH), 123.3 (CH), 122.8 (CH), 120.6 (CH), 108.0 (CH), 107.7 (CH), 100.9 (CH_2), 95.8 (C), 71.0 (CH_2), 70.5 (CH_2), 66.0 (CH), 55.6 (C), 49.1 (CH_2), 34.4 (CH_2), 30.1 (C), 22.9 (CH_3), 22.5 (CH_3), 14.7 (CH_3). ν_{max} 2956, 2869, 1545, 1484, 1372, 1357, 1238, 1166, 1096, 1039, 911, 729, 604 cm^{-1}. *m/z* (ESI, +ve) 577 [$(M+Na)^+$, 100%], 555 [$(M+H)^+$, 98], 469 (35), 267 (39).

Compound ***41***

A magnetically stirred mixture of enyne **19** (86 mg, 0.168 mmol), $Pd(OAc)_2$ (11.3 mg, 0.05 mmol), and BBEDA (11.9 mg, 0.05 mmol) in dry toluene (8.4 mL) was heated at 110°C under an atmosphere of argon for 6 h. The reaction mixture was then cooled and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.4 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***41*** (47 mg, 55%) as a pale-yellow and foamy solid lacking a distinct melting point [Found: $(M+Na)^+$, 535.1151. $C_{25}H_{24}N_2O_8S$ requires $(M+Na)^+$, 535.1151]. δ_H (400 MHz) 7.95 (dd, *J* 8.0 and 1.4, 1H), 7.63 (td, *J* 7.6 and 1.6, 1H), 7.56 (td, *J* 7.6 and 1.2, 1H), 7.52 (dd, *J* 8.0 and 1.6, 1H), 6.93 (s, 1H), 6.89 (s, 1H), 5.97 (d, *J* 1.2, 1H), 5.94 (d, *J* 1.2, 1H), 5.91 (ddd, *J* 10.0, 4.8, and 2.8, 1H), 5.26 (d, *J* 9.6, 1H), 4.98 (m, 1H), 4.69 (d, *J* 2.8, 1H), 4.34 (d, *J* 14.4, 1H), 4.21 (dt, *J* 14.4 and 2.0, 1H), 3.51 (s, 3H), 2.22–2.15 (complex m, 2H), 2.01 (m, 1H), 1.61 (m, 1H), 1.53 (d, *J* 6.8, 3H). δ_C (100 MHz) 168.8 (C), 148.8 (C), 148.6 (C), 146.0 (C), 142.6 (C), 137.9 (C), 132.9 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 127.4 (CH), 125.6 (C), 123.4 (CH), 117.1 (CH), 111.5 (CH), 110.1 (CH), 101.8 (CH_2), 65.4 (CH), 55.5 (C), 51.8 (CH_3), 51.3 (CH_2), 22.9 (CH_2), 20.1 (CH_2), 14.3 (CH_3) (one signal obscured or overlapping). ν_{max} 3022, 2949, 2915, 1723, 1545, 1505, 1487, 1435, 1355, 1253, 1168, 1125, 1037, 734 cm^{-1}. *m/z* (ESI, +ve) 535 [$(M+Na)^+$, 100%], 513 [$(M+H)^+$, 30], 279 (45).

Compound ***42***

A magnetically stirred mixture of enyne **31** (91 mg, 0.15 mmol), $Pd(OAc)_2$ (10 mg, 0.045 mmol), and BBEDA (10.5 mg, 0.045 mmol) in dry toluene (7.4 mL) was heated at 110°C under an atmosphere of argon for 5 h and then cooled and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica gel, 1/3 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.5 in 1/1 v/v ethyl acetate/hexane), the *title compound* ***42*** (83 mg, 92%) as colourless crystals, mp 210–217°C [Found: $(M+Na)^+$, 635.1660. $C_{30}H_{32}N_2O_{10}S$ requires $(M+Na)^+$, 635.1675]. δ_H (400 MHz) 8.08 (m, 1H), 7.66 (m, 2H), 7.53 (m, 1H), 7.26 (s, 1H), 7.16 (s, 1H), 5.99 (m, 2H), 5.02 (dd, *J* 17.4 and 10.6, 1H), 4.87 (dd, *J* 10.0 and 1.1, 1H), 4.83 (dd, *J* 3.2 and 1.1, 1H), 4.67 (d, *J* 3.6, 1H), 4.27 (d, *J* 9.4, 1H), 3.71 (d, *J* 9.4, 1H), 3.60–3.55 (complex m, 2H), 3.51 (d, *J* 11.5, 1H), 3.43 (s, 3H), 3.35 (dd, *J* 11.5 and 1.4, 1H), 2.56–2.48 (complex m, 2H), 2.07 (dd, *J* 15.6 and 4.4, 1H), 1.77 (dd, *J* 14.8 and 6.8, 1H), 1.50 (m, 1H), 1.11 (s, 3H), 0.83 (s, 3H). δ_C (100 MHz) 165.6 (C), 150.6 (C), 148.9 (C), 146.8 (C), 136.2 (CH), 134.3 (C), 133.0 (CH), 131.5 (CH), 130.8 (CH), 124.8 (C), 123.5 (CH), 113.9 (CH_2), 113.4 (CH), 110.2 (CH), 101.8 (CH_2), 98.5 (C), 70.3 (CH_2), 69.9 (CH_2), 62.9 (CH), 52.3 (CH_2), 51.8 (CH_3), 41.4 (C), 38.3 (C), 33.9 (CH_2), 30.0 (C), 29.6 (C), 26.9 (CH_2), 25.9 (CH), 22.7 (CH_3), 22.3 (CH_3). ν_{max} 3084, 3064, 2952, 2926, 2856, 1725, 1545, 1505, 1488, 1374, 1353, 1254, 1170, 1131, 1103, 1038, 909, 738 cm^{-1}. *m/z* (ESI, +ve) 635 [$(M+Na)^+$, 69%], 613 [$(M+H)^+$, 41], 595 (69), 426 (100).

X-ray Crystallographic Studies

Data for Compound ***28***

$C_{27}H_{28}N_2O_8S$, *M* 540.59, *T* 200 K, triclinic, space group $P\bar{1}$, *Z* 2, *a* 10.0669(2), *b* 10.9365(3), *c* 12.8103(3) Å, α 74.2505(11)°, β 72.7388(12)°, γ 81.0724(17)°, *V* 1292.00(5) $Å^3$, D_x 1.390 g cm^{-3}, 7544 unique data ($2\theta_{max}$ 60°), *R* 0.036 [for 6404 reflections with $I > 2.0\sigma(I)$]; *Rw* 0.095 (all data), *S* 1.00.

Data for Compound ***37***

$C_{23}H_{23}NO_4S$, *M* 409.51, *T* 200 K, monoclinic, space group $P2_1/n$, *Z* 4, *a* 10.1955(1), *b* 8.6479(1), *c* 22.2545(2) Å, β 95.5065(8)°, *V* 1953.12(3) $Å^3$, D_x 1.393 g cm^{-3}, 4443 unique data ($2\theta_{max}$ 55°), *R* 0.032 [for 3604 reflections with $I > 2.0\sigma(I)$]; *Rw* 0.092 (all data), *S* 0.95.

Data for Compound ***39***

$C_{23}H_{22}N_2O_6S$, *M* 454.50, *T* 200 K, orthorhombic, space group *Pbca*, *Z* 8, *a* 15.3175(3), *b* 13.3614(2), *c* 21.0221(4) Å, *V* 4302.45(13) $Å^3$, D_x 1.403 g cm^{-3}, 3770 unique data ($2\theta_{max}$ 50°), *R* 0.064 [for 3070 reflections with $I > 2.0\sigma(I)$]; *Rw* 0.170 (all data), *S* 0.99.

Data for Compound ***42***

$C_{30}H_{32}N_2O_{10}S \cdot 2CH_2Cl_2$, *M* 782.52, *T* 200 K, triclinic, space group $P\bar{1}$, *Z* 2, *a* 8.6442(2), *b* 14.8875(5), *c* 15.4877(5) Å, α 116.1546(13)°, β 101.4225(17)°, γ 91.3334(17)°, *V* 1739.70(9) $Å^3$, D_x 1.494 g cm^{-3}, 8004 unique data ($2\theta_{max}$ 55°), *R* 0.053 [for 5959 reflections with $I > 2.0\sigma(I)$]; *Rw* 0.132 (all data), *S* 1.01.

Structure Determination

Images were measured on a Nonius Kappa CCD diffractometer ($Mo_{K\alpha}$, graphite monochromator, λ 0.71073 Å) and data extracted using the *DENZO* package.[23] Structure solution was by direct methods (SIR92).[24] The structure of compounds **28**, **37**, **39**, and **42** were refined using the *CRYSTALS* program package.[25] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos. 790929, 790930, 790931, and 790932 for compounds **28**, **37**, **39**, and **42**, respectively). These data can be obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Accessory Publication

^{1}H and/or ^{13}C NMR spectra for compounds **8**, **10**–**19**, **21**–**31**, **33**, **34**, **37**–**42** are available on the Journal's website.

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References

[1] E. A. Ilardi, M. J. Isaacman, Y.-c. Qin, S. A. Shelly, A. Zakarian, *Tetrahedron* **2009**, *65*, 3261 and references cited therein. doi:10.1016/J.TET.2008.10.048

[2] See, for example, (a) T. Nishimata, Y. Sato, M. Mori, *J. Org. Chem.* **2004**, *69*, 1837. doi:10.1021/JO030309B
(b) F.-M. Zhang, Y.-Q. Tu, J.-D. Liu, X.-H. Fan, L. Shi, X.-D. Hu, S.-H. Wang, Y.-Q. Zhang, *Tetrahedron* **2006**, *62*, 9446. doi:10.1016/J.TET.2006.07.027
(c) C. Bru, C. Guillou, *Tetrahedron* **2006**, *62*, 9043. doi:10.1016/J.TET.2006.07.005
(d) N. T. Tam, J. Chang, E.-J. Jung, C.-G. Cho, *J. Org. Chem.* **2008**, *73*, 6258. doi:10.1021/JO8008353
(e) J.-D. Liu, S.-H. Wang, F.-M. Zhang, Y.-Q. Tu, Y.-Q. Zhang, *Synlett* **2009**, 3040.
(f) A. D. Findlay, M. G. Banwell, *Org. Lett.* **2009**, *11*, 3160. doi:10.1021/OL901230W

[3] See, for example, (a) J. H. Rigby, A. Cavezza, M. J. Heeg, *J. Am. Chem. Soc.* **1998**, *120*, 3664. doi:10.1021/JA974317J
(b) S. W. Baldwin, J. S. Debenham, *Org. Lett.* **2000**, *2*, 99. doi:10.1021/OL9911472

[4] See, for example, (a) H. Ishibashi, N. Uemura, H. Nakatani, M. Okazaki, T. Sato, N. Nakamura, M. Ikeda, *J. Org. Chem.* **1993**, *58*, 2360. doi:10.1021/JO00061A005
(b) T. Nishimata, M. Mori, *J. Org. Chem.* **1998**, *63*, 7586. doi:10.1021/JO9815249
(c) S.-I. Iwamatsu, K. Matsubara, H. Nagashima, *J. Org. Chem.* **1999**, *64*, 9625. doi:10.1021/JO9912146
(d) A. Padwa, M. A. Brodney, M. Dimitroff, B. Liu, T. Wu, *J. Org. Chem.* **2001**, *66*, 3119 and references cited therein. doi:10.1021/JO010020Z

[5] See, for example, (a) M. T. Jones, B. D. Schwartz, A. C. Willis, M. G. Banwell, *Org. Lett.* **2009**, *11*, 3506. doi:10.1021/OL901364N
(b) M. G. Banwell, X. Ma, O. P. Karunaratne, A. C. Willis, *Aust. J. Chem.* **2010**, *63*, 1437. doi:10.1071/CH10201

[6] (a) C. F. Murphy, W. C. Wildman, *Tetrahedron Lett.* **1964**, *5*, 3857 (structure elucidation). doi:10.1016/S0040-4039(01)93306-4
(b) K. Isobe, J. Taga, Y. Tsuda, *Tetrahedron Lett.* **1976**, *17*, 2331 (synthesis). doi:10.1016/S0040-4039(00)78769-7

[7] (a) H. Ishibashi, H. Nakatani, S. Iwami, T. Sato, N. Nakamura, M. Ikeda, *J. Chem. Soc. Chem. Commun.* **1989**, 1767. doi:10.1039/C39890001767
(b) S. W. Baldwin, J. Aubé, A. T. McPhail, *J. Org. Chem.* **1991**, *56*, 6546. doi:10.1021/JO00023A019

[8] For useful descriptions of the Alder–ene reaction, including metal-catalyzed processes, see: (a) B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34. doi:10.1021/AR00170A004
(b) A. Goeke, M. Sawamura, R. Kuwano, Y. Ito, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 662. doi:10.1002/ANIE.199606621
(c) A. Lei, M. He, X. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 8198. doi:10.1021/JA020052J
(d) L. Kürti, B. Czakó, *Strategic Applications of Named Reactions in Organic Synthesis* **2005**, pp. 6–7 (Elsevier Academic Press: Burlington, MA) and references cited therein.

[9] M. G. Banwell, D. A. S. Beck, P. C. Stanislawski, M. O. Sydnes, R. M. Taylor, *Curr. Org. Chem.* **2005**, *9*, 1589 and references cited therein. doi:10.2174/138527205774370469

[10] (a) M. G. Banwell, C. J. Cowden, *Aust. J. Chem.* **1994**, *47*, 2235. doi:10.1071/CH9942235
(b) M. G. Banwell, C. J. Cowden, R. W. Gable, *J. Chem. Soc., Perkin Trans. 1* **1994**, 3515. doi:10.1039/P19940003515

[11] J. Demaison, A. G. Császár, I. Kleiner, H. Møllendal, *J. Phys. Chem. A* **2007**, *111*, 2574. doi:10.1021/JP067278J

[12] (a) H. M. M. Bastiaans, J. L. van der Baan, H. C. J. Ottenheijm, *J. Org. Chem.* **1997**, *62*, 3880 and references cited therein. doi:10.1021/JO961447M
(b) A. J. Zhang, D. H. Russell, J. Zhu, K. Burgess, *Tetrahedron Lett.* **1998**, *39*, 7439. doi:10.1016/S0040-4039(98)01631-1

[13] (a) R. L. Beddoes, L. Dalton, J. A. Joule, O. S. Mills, J. D. Street, C. I. F. Watt, *J. Chem. Soc., Perkin Trans. 2* **1986**, 787. doi:10.1039/P29860000787
(b) M. C. Menziani, M. Cocchi, P. G. De Benedetti, *J. Mol. Struct. THEOCHEM* **1992**, *256*, 217 and references cited therein. doi:10.1016/0166-1280(92)87168-Y
(c) J. Cobb, I. N. Demetropoulos, D. Korakas, S. Skoulika, G. Varvounis, *Tetrahedron* **1996**, *52*, 4485. doi:10.1016/0040-4020(96)00096-8
(d) Y. Zhao, M. Helliwell, J. A. Joule, *J. Chem. Res. (S)* **1999**, 312. doi:10.1039/A809533G

[14] T. Fukuyama, C.-K. Jow, M. Cheung, *Tetrahedron Lett.* **1995**, *36*, 6373. doi:10.1016/0040-4039(95)01316-A

[15] N. Miyaura, T. Yanagi, A. Suzuki, *Synth. Commun.* **1981**, *11*, 513. doi:10.1080/00397918108063618

[16] M. G. Banwell, X. Ma, R. M. Taylor, A. C. Willis, *Org. Lett.* **2006**, *8*, 4959. doi:10.1021/OL062020X

[17] J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312. doi:10.1021/JA016431E

[18] L. Xu, U. H. Brinker, in *Synthetic Organic Sonochemistry* **1998**, pp. 344–345 (Ed. J.-L. Luche) (Plenum Press: New York, NY).

[19] B. M. Trost, C. Pedregal, *J. Am. Chem. Soc.* **1992**, *114*, 7292. doi:10.1021/JA00044A049

[20] C. Yang, S. P. Nolan, *J. Org. Chem.* **2002**, *67*, 591. doi:10.1021/JO010837S

[21] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923. doi:10.1021/JO00408A041

[22] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518. doi:10.1021/OM9503712

[23] DENZO–SMN: Z. Otwinowski, W. Minor, Processing of X-ray diffraction data collected in oscillation mode, in *Methods in Enzymology, Volume 276: Macromolecular Crystallography, Part A* **1997**, pp. 307–326 (Eds C. W. Carter Jr, R. M. Sweet) (Academic Press: New York, NY).

[24] SIR92: A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Cryst.* **1994**, *27*, 435.

[25] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout, D. J. Watkin, *J. Appl. Cryst.* **2003**, *36*, 1487. doi:10.1107/S0021889803021800