A radical based addition–elimination route for the preparation of indoles

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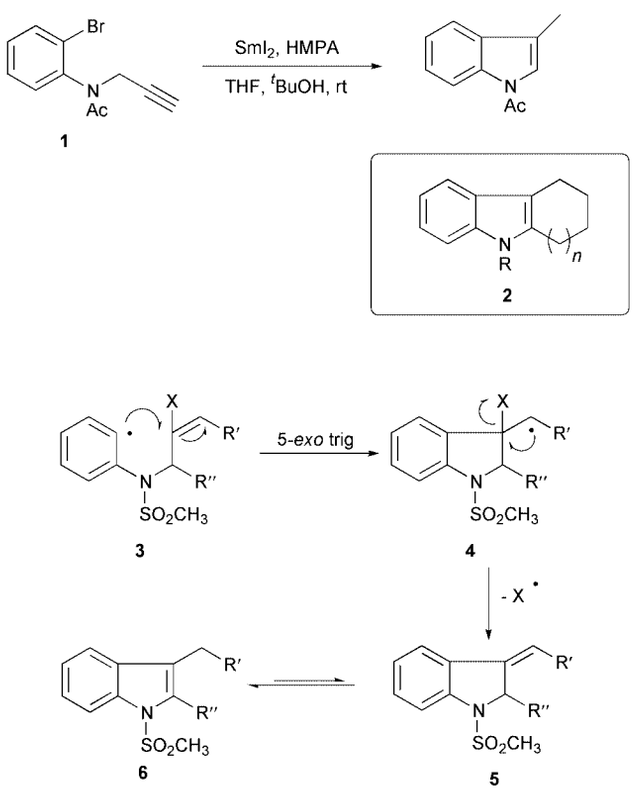
Indoles, including tricyclic derivatives, are produced by cyclisations of aryl radicals onto vinyl halides followed by elimination of halide radical and tautomerism of the resulting product; the aryl radicals are produced using "clean methodology" either by reaction of iodide ions with arenediazonium salts or by reaction of phosphorus-centred radicals with aryl iodides.

Introduction

The preparation of the indole nucleus has inspired numerous different synthetic approaches, but, surprisingly, few use the chemistry of free radicals.[1–4] A notable recent exception is depicted in Scheme 1[2] featuring cyclisation onto the alkyne **1**.



Scheme 1

This example provides a background for our study. The current drive to make radical chemistry more environmentally acceptable would preclude the use of the radioactive samarium diiodide or a carcinogenic reagent like hexamethylphosphoramide. Our wish was to extend the scope of radical approaches to the synthesis of indoles to include alternative methods of radical generation. Furthermore, indoles in which the pyrrole ring is fused to another ring *e.g.* **2**, $n = 0$, 1, 2, could not be generated in this manner since an alkyne cannot be conveniently present in a ring smaller than eight atoms.

Accordingly, our proposal envisaged[5] a very direct and simple addition–elimination route to indoles involving 5-*exo-trig* cyclisation of an aryl radical **3** (generated from the corresponding arenediazonium salt or aryl iodide) onto a suitably substituted olefin to give alkyl radical **4**. Then, if X is a good radical leaving group, β-elimination should occur resulting in the formation of the exocyclic alkene **5**, which should possess a strong driving force to tautomerise to its more stable aromatic tautomer, the indole **6**. This approach should permit simple access to a very wide range of indoles including the tricyclic indoles **2**.

Discussion

Two considerations are central to this work: (i) the method of radical generation and (ii) the nature of the leaving group in the addition–elimination reaction. To make radical chemistry applicable to pharmaceutical preparation, it is necessary that tin-based methods are avoided, and extensive research is underway in this area.[6] This consideration governed our selection of two methods for radical generation. Arenediazonium salts[7] afford aryl radicals when reacted with electron donors, and this has recently been used for extensive studies on the tetrathiafulvalene-triggered radical–polar crossover reaction.[7a] The second method involved aryl iodides, which are converted to aryl radicals on reaction with AIBN and hypophosphorous acid[8] and its salts. This method has recently been used for the formation of carbon–carbon bonds, and Fukuyama *et al.* have elegantly deployed[4c,d] the method for the formation of indoles. However their approach is quite different from that proposed here, involving thioamides **7** as substrates (Scheme 2).

Selection of these methods in turn influenced our choice of leaving group, X$^{\bullet}$. For the aryl iodide reactions, it is appropriate to choose bromine as the leaving group, since it has been shown that aryl carbon–bromine bonds are far less reactive to the phosphorus-centred radicals than aryl carbon–iodine bonds;[4,8] extrapolation suggests that vinyl bromides should also be relatively unreactive. The alternative leaving groups which were considered were sulfur leaving groups, *i.e.* thiyl, sulfenyl and

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sulfinyl radicals arising from the corresponding sulfide, sulfoxide and sulfone respectively.[9] Hypophosphorous acid is a dibasic acid, and its commerically available *N*-ethylpiperidine salt is still a monobasic acid, so the most acid-sensitive of the three groups, the vinyl sulfide was not selected. A vinyl sulfone was ultimately selected, and its synthesis and reactions are described below.

In planning the use of arenediazonium salts as aryl radical precursors, the vinyl sulfones are not so appropriate, since the diazonium salt would be prepared from the corresponding amine **8**, and such an amine could undergo intermolecular or intramolecular nucleophilic attack on the vinyl sulfone. On the other hand, vinyl bromides appeared quite appropriate radicophiles for the diazonium salt substrates.

Vinyl sulfone substrate 15

The target indole was *N*-methylsulfonyl-3-methylindole **11** which might be produced by the cyclisation shown in Scheme 3. Although possible complications with the regiochemistry of cyclisation could arise, we were confident that the 5-*exo*-cyclisation should be more rapid than the potential 6-*endo* alternative in the light of the work of Harvey and Whitham[10] who had shown that **9** afforded **10** selectively. Aryl radicals are normally more selective than alkyl radicals for 5-*exo* over 6-*endo* cyclisation.

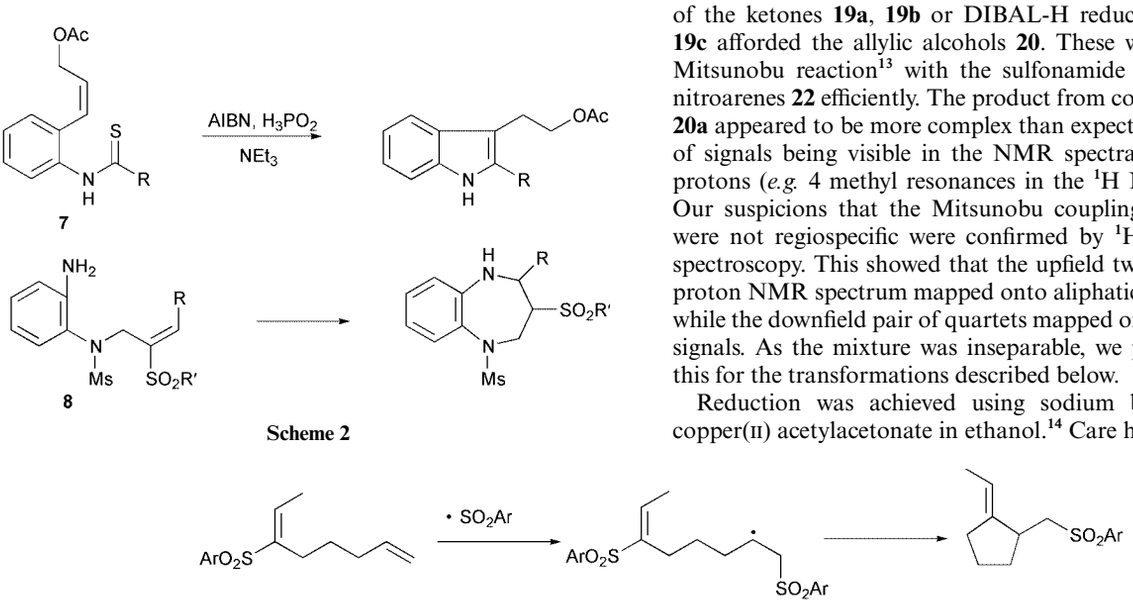
To prepare the desired diazonium salt, allyl methyl sulfide **12** was converted to the intermediate dibromo compound, which was then oxidised to the corresponding sulfone **13** using MCPBA.[11] Subsequent elimination of hydrogen bromide from this intermediate compound was effected with sodium acetate at ambient temperature, affording the desired 1-(bromomethyl)-vinyl methyl sulfone **14** in 48% over three steps from **12**.

Coupling of *N*-(2-iodophenyl)methanesulfonamide **16** with 1-(bromomethyl)vinyl methyl sulfone **14**, afforded **15** (47%). This compound showed restricted rotation in its ^{1}H NMR spectrum where the two protons of the CH_2 group resonated at δ 4.57 and 4.91. This restricted rotation was a general feature of the *N*-alkyl *o*-nitro- (or *o*-iodo)-arenesulfonamides in this study. Sulfonamide **15** was then reacted with *N*-ethylpiperidine hypophosphite (EPHP) and AIBN. This did not afford the expected indole, however, but rather the iodophenylmethanesulfonamide **16** and its de-iodinated analogue. No sulfone-containing product was isolated. The observed fragmentation may have occurred either by addition of a phosphorus radical to the unsubstituted alkene terminus in **15** followed by loss of the arenesulfonamidyl radical—or by attack of hypophosphite anion as a nucleophile expelling the sulfonamide anion. Hence, it was clear that exploring the chemistry of vinyl sulfones was not the best way forward, and so, vinyl bromides were explored.

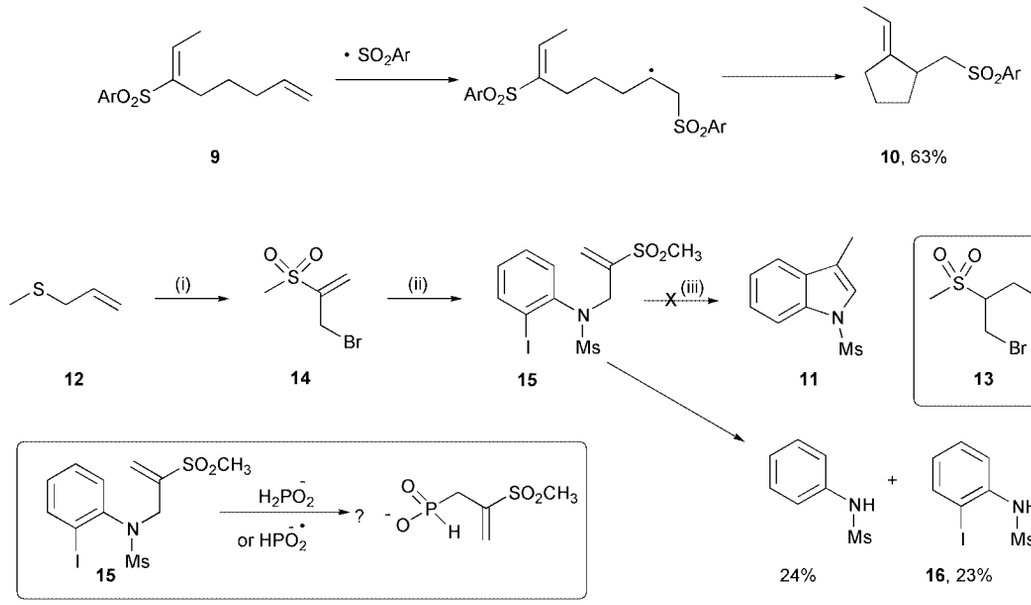
Vinyl bromide substrates

Initially, three simple substituted vinyl bromides **17a**–**c** were selected for synthesis (Scheme 4). Bromination of alkenes **18** was effected using 0.9 equiv. of bromine at −10 °C, the low temperature being required in order to minimise side-reactions. Dehydrobromination of the intermediate dibromo compound occurred cleanly on treatment with base. Luche reduction[12] of the ketones **19a**, **19b** or DIBAL-H reduction of the ester **19c** afforded the allylic alcohols **20**. These were subjected to Mitsunobu reaction[13] with the sulfonamide **21** affording the nitroarenes **22** efficiently. The product from coupling of alcohol **20a** appeared to be more complex than expected, with four sets of signals being visible in the NMR spectra for many of its protons (*e.g.* 4 methyl resonances in the ^{1}H NMR spectrum). Our suspicions that the Mitsunobu coupling of this alcohol were not regiospecific were confirmed by ^{1}H–^{13}C correlation spectroscopy. This showed that the upfield two quartets in the proton NMR spectrum mapped onto aliphatic methine signals, while the downfield pair of quartets mapped onto vinyl methine signals. As the mixture was inseparable, we proceeded to use this for the transformations described below.

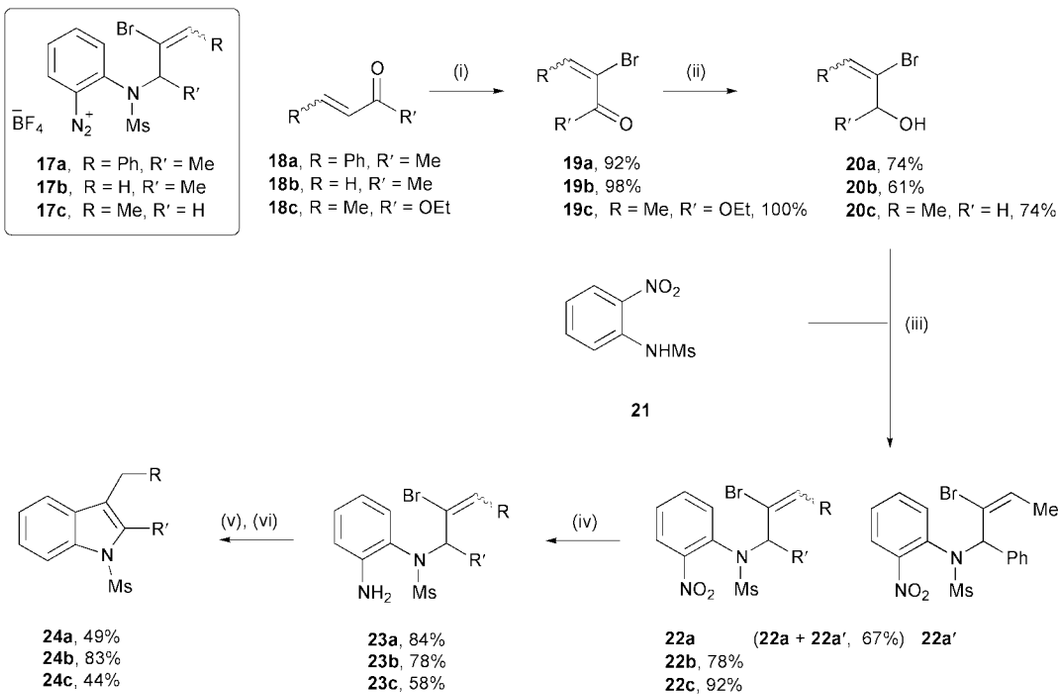
Reduction was achieved using sodium borohydride and copper(II) acetylacetonate in ethanol.[14] Care had to be taken at



Scheme 2



Scheme 3 *Reagents and conditions*: (i) Br_2, CCl_4, −10 °C→rt, 15 min, then MCPBA, −10 °C to rt, 6 h, then NaOAc, Et_2O, rt, 48%; (ii) NaH, IC_6H_4NHMs (**16**), DMF, rt, 47%; (iii) AIBN, EPHP, PhH, reflux.



Scheme 4 *Reagents and conditions*: (i) Br_2, CCl_4, −10 °C, then Et_3N, CH_2Cl_2, rt; (ii) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, 0 °C for conversion of **19a**, **19b**, DIBAL-H, THF, −78 °C for conversion of **19c**; (iii) DEAD, Ph_3P, THF, 0 °C; (iv) $NaBH_4$, $Cu(acac)_2$, EtOH, rt; (v) $NOBF_4$, CH_2Cl_2, rt; (vi) NaI, AR acetone, rt.

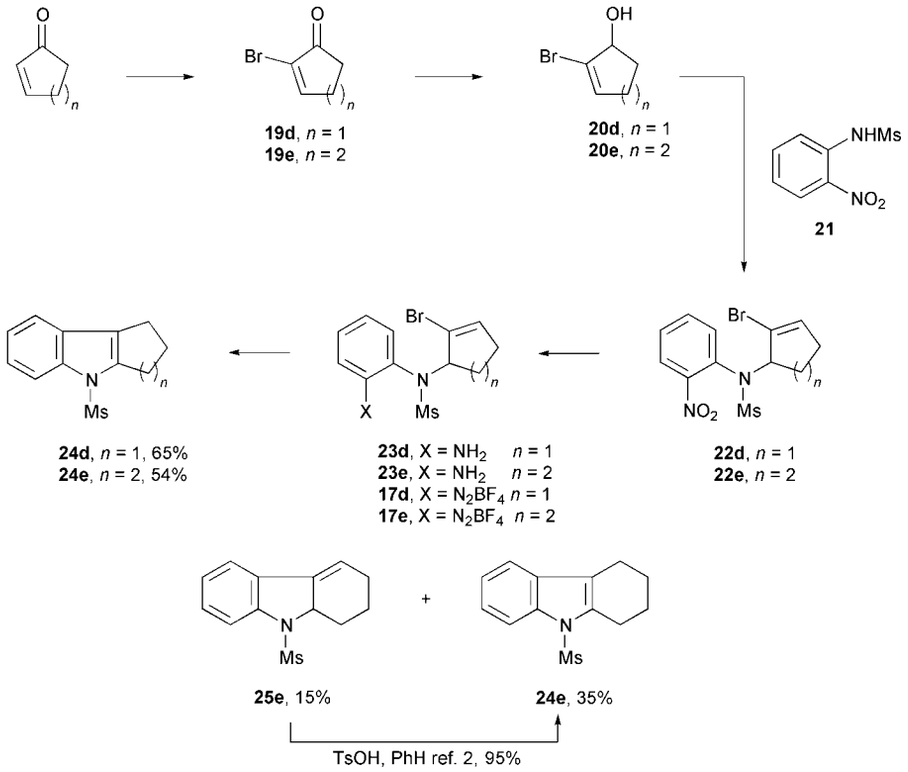
this stage to ensure reduction of the olefin was avoided. Thus, if any starting material was still present by TLC analysis (even after longer reaction times) then, rather than adding more sodium borohydride, the reaction was simply worked up and the two compounds separated by column chromatography. It should also be noted that washing the organic extracts of the reaction mixture with ammonia solution during work-up allowed the facile removal of any copper residues that were often otherwise difficult to remove from the desired compound, even by column chromatography. It was noteworthy that the NMR spectrum of the purified amine **23a** was simpler than its precursor nitro compound; for example, only two doublets were present for its CH–CH_3 methyl group (4 doublets had been present at the preceding nitro stage which had comprised **22a** and **22a′**). The chemical shifts were consistent with pure **23a** rather than the reduction product of **22a′**.

The aryl amines **23** were subsequently subjected to diazotisation. This procedure gave dry diazonium salts **17**, and as such was preferred to the aqueous fluoroboric acid and sodium nitrite conditions used by Beckwith and Meijs.[7f] The intermediate diazonium salts were isolated simply by evaporation of the reaction solvent and treated with sodium iodide to induce radical cyclisation[7f] onto the pendant vinyl bromide. A vigorous evolution of gas accompanied this reaction which afforded the indole products **24** directly when prolonged reaction times were used, tautomerism occurring *in situ*.

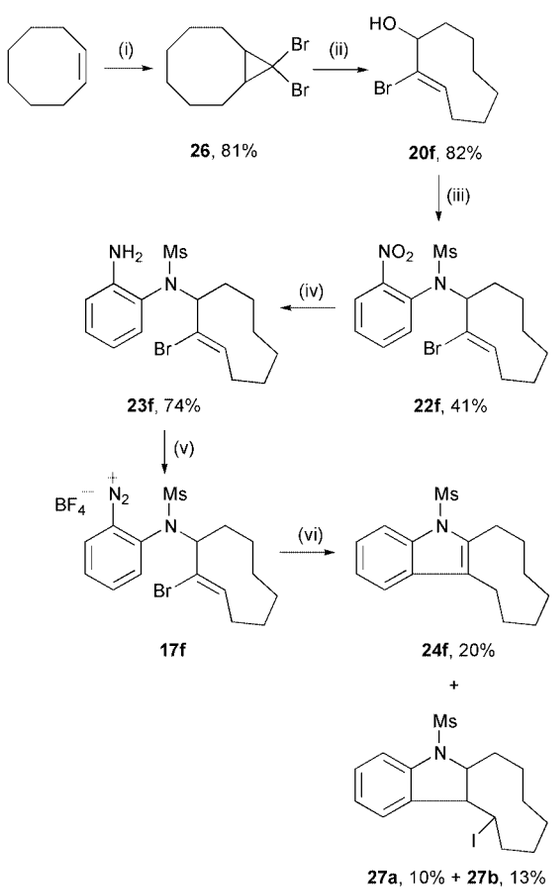
Having completed the synthesis of the simple indoles, attention focused on the more complex tricyclic products **24d** and **24e** (Scheme 5). The precursor diazonium salts were prepared from cyclohexenone and cyclopentenone in an analogous manner to the previous examples. Restricted rotation was seen in compounds **22d** and **22e** by ^{1}H NMR, with the two rotamers being present in these compounds in ratios of 2:1 and 7:1 respectively. Compound **22e** afforded the indole product (54%) following tautomerisation. However, the exocyclic alkene intermediate **25e** could be isolated when the reaction was worked up immediately after adding the iodide ion. Thus the intermediate **25e** was isolated in 15% yield, as well as the desired indole **24e** in 35% yield. The alkene **25e** was then efficiently converted to the indole **24e** by treatment with acid. The combined yield of indole by this method was thus 49%.

Attention now turned to the synthesis of indole **24f** (Scheme 6). This molecule was of interest because the important anticancer drugs vinblastine[15] and vincristine contain such a system where the fused-ring is nine-membered. Since cyclonon-2-en-1-one is not commercially available, and seemed difficult to prepare, the alcohol, **20f**, required for the Mitsunobu reaction was prepared by the known procedure from 9,9-dibromobicyclo-[6.1.0]nonane **26**, using a silver ion-promoted ring expansion.[16]

The ^{1}H NMR spectrum of alcohol **20f** was intriguing, since it showed three sets of peaks for every proton. The smallest peak (~7% by ^{1}H NMR) represents the (*E*)-isomer. The other two peaks (37% and 56%) represent the (*Z*)-isomer, which existed as two separate conformers at room temperature. This result is in agreement with the previously reported analysis of this compound.[16] The isomers of the alcohol could not be separated, but in principle this did not pose a problem, since all the isomers should react to give the same intermediate radical during the final cyclisation. The Mitsunobu reaction to form **22f** was initially attempted using triphenylphosphine and diethyl azodicarboxylate (DEAD) in THF at 0 °C, but only a trace amount of the nitro product was obtained. The reaction was then repeated using the smaller phosphine, diphenyl(methyl)phosphine, and a significant increase in yield was seen (16%). Again, purification of the nitro compound proved to be difficult and time-consuming, but eventually gave microanalytically pure crystals. Surprisingly, the ^{1}H NMR spectrum was very simple to interpret, and showed the presence of only one "isomer" of the nitro product **22f**, the isomer being one form of the (*Z*)-isomer. Even more interestingly, some alcohol **20f** (41%) was recovered from the reaction, and the relative proportions of the alcohol isomers had changed, with the major (*Z*)-isomer now present at 82% (56% before the reaction), the minor form of the (*Z*)-isomer present at only 14% (37% prior to reaction), and the (*E*)-isomer present at 4% (7% before the reaction). This indicates that the Mitsunobu reaction was preferentially taking place *via* one isomer of the (*Z*)-alkene. It was therefore thought that higher temperatures might effect the conversion of the major (*Z*)-conformer to the minor (*Z*)-conformer, thus allowing coupling to take place. Alternatively, the increased temperature should allow the less reactive (*Z*)-conformer or the (*E*)-isomer to become more reactive. As a result, the reaction



Scheme 5



Scheme 6 *Reagents and conditions*: (i) Br_3CH, KO*t*-Bu, hexane, 0 °C; (ii) $AgClO_4$, H_2O, acetone, 0 °C; (iii) DEAD, Ph_2MeP, THF, (**21**), 0 °C then Δ; (iv) $Cu(acac)_2$, $NaBH_4$, EtOH, 0 °C; (v) $NOBF_4$, DCM, 0 °C; NaI, acetone.

was repeated, this time with heating. The reagents were added at 0 °C, and then the solution was allowed to warm to room temperature and stirred for 30 minutes, before being heated to reflux. Pleasingly, a substantial increase in the yield of the nitro compound **22f** was seen (41%). Copper acetylacetonate–sodium borohydride–ethanol was used to reduce the nitro compound **22f** to the desired aniline **23f** (74% yield).

The ^{1}H NMR and ^{13}C NMR spectra of **23f** were complicated, which was surprising, because the precursor nitro compound **22f** had been present as a single "isomer". Diazotisation of the aniline **23f** was effected using nitrosonium tetrafluoroborate in DCM at 0 °C. The diazonium salt was isolated as a fluffy yellow solid by precipitation in diethyl ether. Unfortunately, the solid started to decolorise and became oily almost immediately, even before the solvent could be removed by decanting. As a result, no yield was obtained, and the salt was immediately taken onto the next stage. Cyclisation was achieved by stirring the diazonium salt in acetone under N_2 at 0 °C with sodium iodide. After work-up, column chromatography gave the desired indole **24f** (20%). Intriguingly, two isomers of the unexpected iodo side-product **27** were also isolated (**27a**, 13% and **27b**, 10%). The identity of the iodo products **27** was initially confusing, because although ^{1}H and ^{13}C NMR spectra, mass spectral analysis and elemental analysis indicated that the structure of each of the two products was consistent with the proposed structure, their mechanism of formation was puzzling. Finally, X-ray crystallography of one of the products confirmed the structure as the 9-membered iodo compound **27a**[17] (Fig. 1).

Compounds **27a** and **27b** may arise following the initial cyclisation giving the desired β-bromoalkyl radical, **28** (Scheme 7). It may be that conformational peculiarities of the nine-membered ring inhibit the desired elimination reaction, allowing the observed alternative reactions to occur.

1,2-Bromine shift reactions of β-bromoalkyl radicals are known in simple substrates,[18] and it is thought that such a rearrangement may have occurred here. This would give a relatively stable benzylic radical, which could then abstract a hydrogen atom from solvent, to give a nine-membered bromo compound, **29**. Displacement of bromide by an iodide anion could then give the iodo product **27**.

Alternatively, after initial cyclisation, loss of a bromine radical could occur as expected, to give the desired alkene inter-

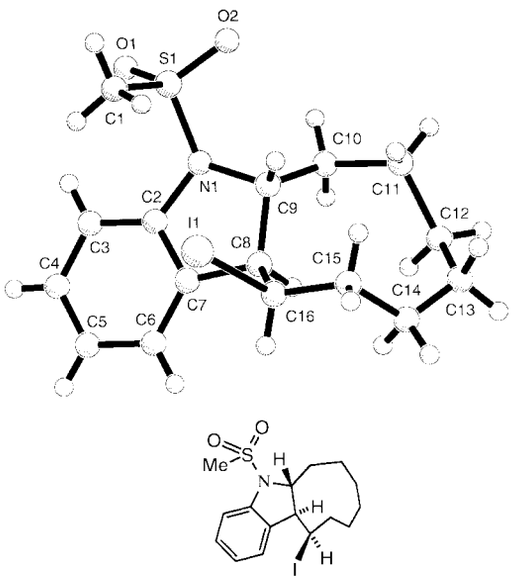
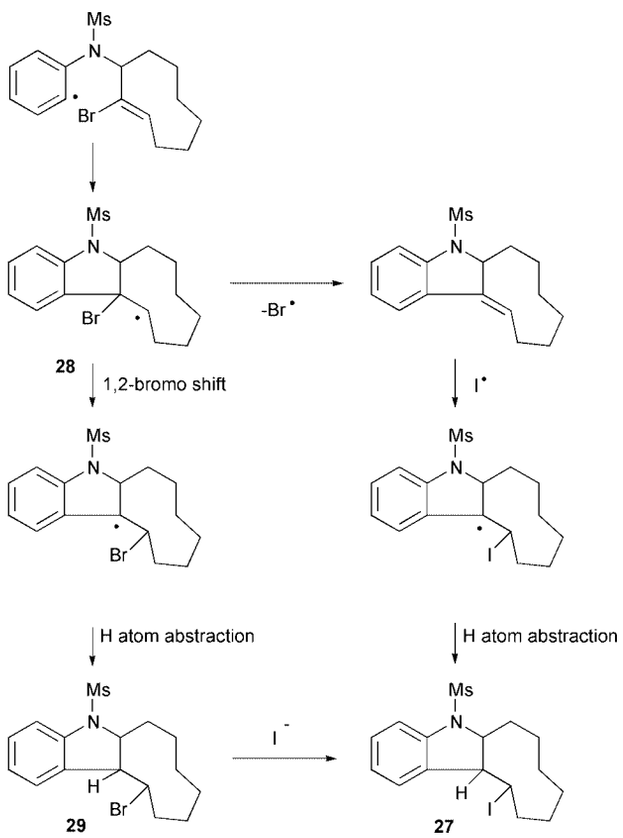


Fig. 1 X-Ray crystal structure of **27a**.

mediate. Then, perhaps due to conformational peculiarities of the nine-membered ring, the intermediate might be attacked by iodine atoms, again giving relatively stable benzylic radicals. Abstraction of a hydrogen atom would be required to form the iodo product **27**. The two proposed mechanisms are given in Scheme 7.



Scheme 7

Having successfully prepared these indoles using diazonium salts as precursors, attention moved towards the synthesis of aryl iodides and their cyclisation using tributyltin radicals. Coupling of the alcohol **20e** with the *N*-mesyl derivative of iodoaniline **16** was achieved using Mitsunobu conditions. The product, **30**, was firstly treated with *N*-ethylpiperidine hypophosphite (EPHP), and the radical initiator, AIBN (Scheme 8). The alkene **25e** was isolated in 60% yield, along with recovered starting material. Acid-catalysed conversion of the alkene **25e** to the desired indole **24e** occurred in high yield (94%). The successful formation of indole **24e** confirmed the potential of the phosphorus reagents in this new synthesis.

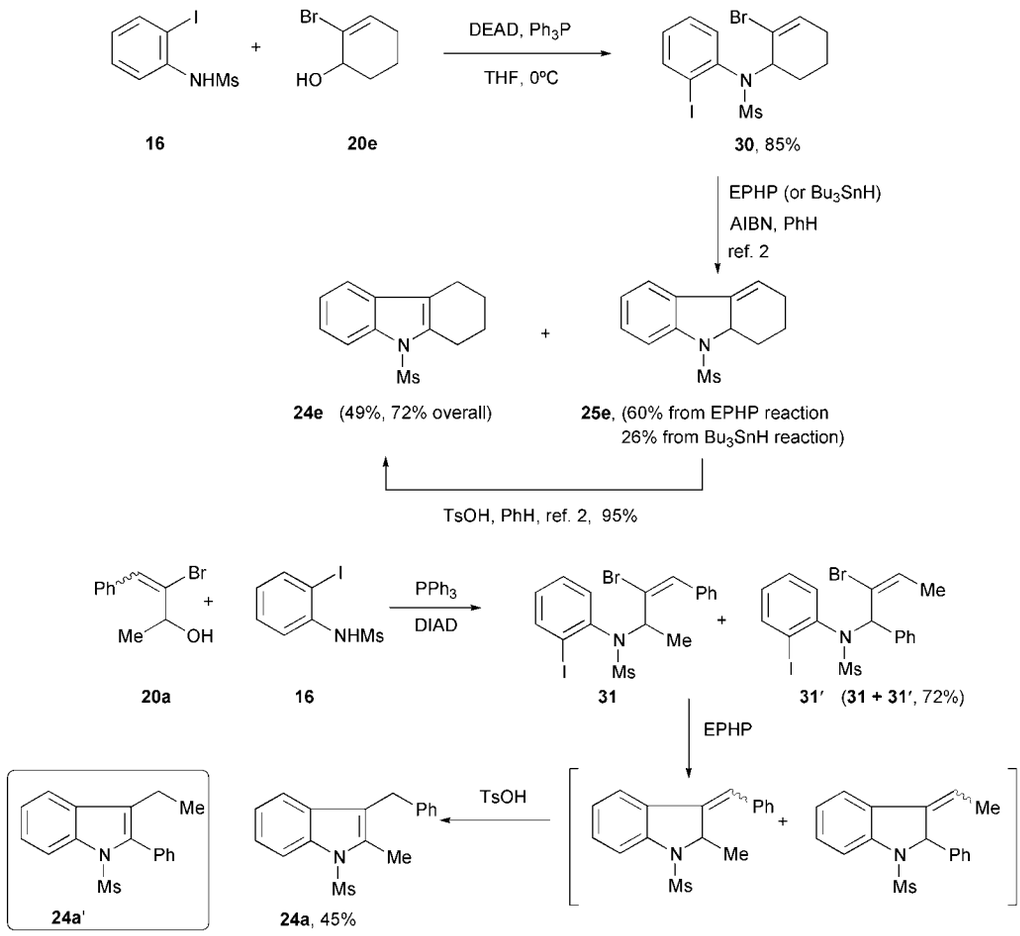
For comparison, the radical cyclisation was repeated, this time using tributyltin hydride as reagent (and using a full equivalent of AIBN, since this reaction may not be a chain reaction). The desired indole **24e** was isolated in 49% yield, along with the intermediate unrearranged alkene **25e**, which was isolated in 26% yield. Acid-catalysed conversion of the alkene **25e** to the desired indole **24e** occurred in high yield, giving the indole in 72% overall yield. Although the tin reagent gives a slightly higher yield in the formation of this indole, its toxicity drawbacks remain.

Finally, alcohol **20a** was coupled under Mitsunobu conditions with *N*-(2-iodophenyl)methanesulfonamide **16**. This alcohol had afforded a regioisomeric mixture of Mitsunobu coupling products when coupled with the nitrosulfonamide **21**. A similar result was observed here, and once again four doublets were present for the $CHCH_3$ methyl group and four quartets for the corresponding methine proton. Once again ^1H–^{13}C correlation spectroscopy indicated that two of the quartets were associated with aliphatic carbons and two with vinyl carbons, and so this Mitsunobu reaction afforded a mixture of **31** and **31′**. This inseparable mixture was subjected to cyclisation. When the reaction was first conducted, using AIBN (0.4 equiv.), only a single indole, **24a**, was isolated in 45% yield following tautomerism induced by toluene-*p*-sulfonic acid. Because we were uncertain that the radical reaction would proceed by a proper chain mechanism in which bromine atoms abstract a hydrogen from tributyltin hydride, the experiment was repeated with a full equivalent of AIBN. [We recognise that the 0.4 equiv. of AIBN used could afford 0.8 equiv. of isobutyronitrile radicals—but not all of these would be used in initiating the desired reaction by abstraction of hydrogen from tributyltin hydride]. This led to a decrease in yield of indole **24a** (41%), but the elusive isomeric indole **24a′** was isolated in low yield (4%).

In conclusion, an addition–elimination strategy has been used to prepare indole products by radical methodology using arenediazonium salts and using phosphorus-centred radicals. The methods used avoid the difficulties associated with tributyltin reagents or samarium diiodide.

Experimental

Melting points were measured on a Kofler hot stage apparatus and are uncorrected. Microanalyses were determined using a Perkin-Elmer 240B elemental analyser. Infrared spectra were obtained on a Perkin-Elmer 1720-X FTIR or a Pye-Unicam SP3-100 spectrometer. Ultraviolet spectra were recorded on a Philips PU8700 series instrument. ^1H NMR spectra were recorded at 250 MHz on a Bruker WM250, at 270 MHz on a JEOL EX270 or at 400 MHz on a Bruker DPX400 machine. ^{13}C NMR spectra were recorded at 62.9 MHz on a Bruker WM250, at 67.8 MHz on a JEOL EX270 or at 100 MHz on a Bruker DPX400 machine. NMR experiments were carried out in deuterochloroform, d_4-methanol, or d_6-acetone with tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (ppm). The following abbreviations are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants are reported in hertz (Hz). In cases where superimposition of the signals of two, or more, isomers occurred, the signals have been reported as multiplets (m), unless the coupling constants of each isomer could be ascertained. Mass spectra were recorded at the EPSRC Mass Spectrometry Service Centre, Swansea or using a JEOL JMS-AX505HA at Strathclyde.



Scheme 8

Where necessary, solvents were dried and/or distilled before use. Tetrahydrofuran was distilled from sodium–benzophenone. Dichloromethane and dimethylformamide were distilled from calcium hydride. Diethyl ether, toluene and benzene were dried over sodium wire. Unless otherwise stated all petrol was of boiling range 40–60 °C and was distilled before use. Chromatography was performed using Sorbsil C60 (May and Baker), Kieselgel 60 (Art 9385) or Kieselgel HF254 silica gels.

1-(Bromomethyl)vinyl methyl sulfone 14

To a solution of allyl methyl sulfide **12** (6.7 ml, 60 mmol, 1.0 equiv.) in carbon tetrachloride (160 ml) was added a solution of bromine (3.1 ml, 0.60 mmol, 1.0 equiv.) in carbon tetrachloride (25 ml), dropwise *via* syringe whilst stirring constantly under nitrogen at −10 °C. Once the addition was complete the mixture was allowed to warm to room temperature over a period of 15 min, before cooling to −10 °C again. *m*-Chloroperoxybenzoic acid (25.0 g, 14.5 mmol, 2.4 equiv.) in dichloromethane (120 ml) was added to the mixture a little at a time. Each addition was accompanied by an exotherm to *ca.* 10 °C. The mixture was left to stir at room temperature for 6 h before washing with saturated sodium bicarbonate solution (3 × 300 ml). The organic phase was dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield an off-white solid. To this was added diethyl ether (300 ml) (dried over sodium wire) and the solution treated with sodium acetate (6.15 g, 0.075 mol, 1.5 equiv.). The mixture was stirred under nitrogen at room temperature for 5 h. Ethyl acetate (200 ml) was added and the mixture washed with water (2 × 300 ml). The organic phase was dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a yellow oil. This was purified by column chromatography (silica; 10% hexane in dichloromethane to 100% dichloromethane gradient elution) to yield *1-(bromomethyl)vinyl methyl sulfone* **14** (5.741 g, 0.0288 mol, 48%) as a yellow oil which solidified on cooling, mp 35–36.5 °C (Found: C, 23.9; H, 3.5. $C_4H_7BrO_2S$ requires C, 24.1; H, 3.5%); ν_{max}(KBr disc)/cm^{-1} 3037, 2927 (CH), 1630 (C=C), 1415 (CH), 1321, 1143 (SO_2); δ_H(250 MHz, $CDCl_3$) 3.09 (3H, s, CH_3), 4.29 (2H, s, CH_2), 6.25 (1H, d, *J* 0.9, =CH), 6.45 (1H, d, *J* 0.9, =CH); δ_C(62.9 MHz, $CDCl_3$) 25.8 (CH_2), 43.8 (CH_3), 130.5 (CH_2), 147.0 (C).

2-Iodo-*N*-methylsulfonylaniline 16

2-Iodoaniline (50 g, 228 mmol, 1 equiv.), *N*,*N*-dimethylaminopyridine (2.78 g, 22.8 mmol, 0.1 equiv.) and methanesulfonyl chloride (21.1 ml, 31.24 g, 274 mmol, 1.2 equiv.) were stirred in pyridine (160 ml) under nitrogen and heated under reflux for 18 h. Dichloromethane (400 ml) was added and the mixture was washed with hydrochloric acid (2 M, 3 × 250 ml). The organic solution was then extracted with sodium hydroxide (2 M, 3 × 200 ml). The combined aqueous portions were acidified with conc. hydrochloric acid, and extracted into dichloromethane (3 × 150 ml). The combined organic portions were dried over magnesium sulfate and the solvent removed to give a brown oil. Recrystallisation from ethyl acetate and hexane gave 2-iodo-*N*-methylsulfonylaniline **16** as a pale brown solid (48.96 g, 72%), mp 94–95 °C (Found: C, 28.1; H, 2.4; N, 4.6. $C_7H_8INO_2S$ requires C, 28.3; H, 2.7; N, 4.7%); ν_{max}(KBr disc)/cm^{-1} 3283, 1582; δ_H($CDCl_3$, 400 MHz) 3.02 (3H, s, SO_2CH_3), 6.68 (1H, br s, NH), 6.93 (1H, ddd, *J* 8.0, 7.3, 1.5, ArH), 7.37 (1H, ddd, *J* 8.2, 7.2, 1.4, ArH), 7.64 (1H, dd, *J* 8.2, 1.5, ArH), 7.82 (1H, dd, *J* 8.0, 1.4, ArH); δ_C($CDCl_3$, 100 MHz) 40.4 (CH_3), 92.4 (C), 122.7 (CH), 127.4 (CH), 130.0 (CH), 137.8 (C), 139.6 (CH); *m*/*z* (EI) 297 (M^+, 93%), 218 (100), 91 (89), 64 (60).

N-(2-Iodophenyl)-N-[2-(methylsulfonyl)prop-2-enyl]methanesulfonamide 15

A suspension of sodium hydride (0.091 g, 3.8 mmol, 1.5 equiv.) in dry *N*,*N*-dimethylformamide (10 ml) was treated with a solution of *N*-(2-iodophenyl)methanesulfonamide **16** (0.746 g, 2.5 mmol, 1.0 equiv.) in dry *N*,*N*-dimethylformamide (2 ml), dropwise *via* syringe whilst stirring under nitrogen at room temperature. Bubbles of gas were evolved and the solution became yellow in colour. After 15 min, a solution of 1-(bromomethyl)vinyl methyl sulfone **14** (0.5 g, 2.5 mmol, 1.0 equiv.) in dry *N*,*N*-dimethylformamide (2 ml) was added dropwise *via* syringe while stirring under nitrogen at room temperature. The solution became dark brown in colour. After 4 h, ethyl acetate (40 ml) was added and the mixture washed with water (6 × 40 ml). The organic phase was dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a dark yellow oil. This was purified by column chromatography (silica; 50% ethyl acetate in hexane to 60% ethyl acetate in hexane gradient elution) to afford *N-(2-iodophenyl)-N-[2-(methylsulfonyl)prop-2-enyl]methanesulfonamide* **15** (0.486 g, 1.2 mmol, 47%) as a yellow solid, mp 121–122.5 °C [Found: M^+ (EI), 414.9409. $C_{11}H_{14}O_4NS_2I$ requires *M*, 414.9409]; ν_{max}(KBr disc)/cm^{-1} 3011, 2927, 1478 (CH), 1342 (N–SO_2), 1300 (SO_2), 1159 (N–SO_2), 1133 (SO_2), 798 (Ar ring); δ_H(270 MHz, $CDCl_3$) 2.88 (3H, s, CH_3), 3.15 (3H, s, CH_3), 4.57 (1H, d, *J* 16.7, CH_2), 4.91 (1H, d, *J* 16.7, CH_2), 6.12 (1H, d, *J* 1.1, =CH), 6.45 (1H, br s, =CH), 7.12 (1H, ddd, *J* 8.1, 7.1, 1.6, ArH), 7.42 (1H, ddd, *J* 7.8, 7.1, 1.4, ArH), 7.51 (1H, dd, *J* 7.8, 1.6, ArH), 7.97 (1H, dd, *J* 8.1, 1.4, ArH); δ_C(67.8 MHz, $CDCl_3$) 41.4 (CH_3), 41.5 (CH_3), 49.6 (CH_2), 100.0 (C), 129.7 (CH), 130.1 (CH_2), 131.0 (CH), 133.52 (CH), 140.0 (C), 141.2 (CH), 145.4 (C); *m*/*z* (EI) 415 (M^+, 5%), 336 (57), 256 (55) and 130 (100).

Reaction of 1-ethylpiperidine hypophosphite (EPHP) with N-(2-iodophenyl)-N-[2-(methylsulfonyl)prop-2-enyl]methanesulfonamide 15

EPHP (1.3 g, 7.2 mmol, 10 equiv.) was added to a solution of *N*-(2-iodophenyl)-*N*-[2-(methylsulfonyl)prop-2-enyl]methanesulfonamide (300 mg, 0.72 mmol, 1 equiv.) in dry benzene (8 ml) and the reaction was heated at reflux for 30 min. AIBN (47 mg, 0.3 mmol, 0.4 equiv.) was added in two portions over 30 min and the reaction was refluxed for 1 h. The reaction was cooled before diluting with dichloromethane and extracted with water (50 ml). The organic phase was dried over sodium sulfate and removed under vacuum. The residue obtained was purified by column chromatography (5% ethyl acetate in hexane and gradient elution to 50% ethyl acetate) to afford 2-iodo-*N*-methylsulfonylaniline **16** (45 mg, 0.15 mmol, 23.3%) (data as reported above) and *N*-methylsulfonylaniline (30 mg, 0.17 mmol, 24.3%), δ_H($CDCl_3$, 400 MHz) 3.04 (3H, s, CH_3), 6.94 (1H, br s, NH), 7.19–7.28 (3H, m, ArH), 7.35–7.40 (2H, m, ArH); δ_C($CDCl_3$, 100 MHz) 39.3 (q, CH_3), 120.8 (d), 125.4 (d), 129.7 (d), 136.7 (s).

(E)-3-Bromo-4-phenylbut-3-en-2-one 19a[19]

A solution of bromine (0.63 ml, 0.0122 mol, 0.9 equiv.) in carbon tetrachloride was added dropwise *via* syringe to a solution of (*E*)-4-phenylbut-3-en-2-one **18a** (2.00 g, 0.0136 mol, 1.0 equiv.) in carbon tetrachloride (5 ml) while stirring under nitrogen at −10 °C. The bromine solution was added at a rate that did not allow the temperature to exceed *ca.* −2 °C. As the bromine solution was added it decolorised, and an off-white precipitate formed. Carbon tetrachloride (15 ml) was added during the course of the reaction to aid stirring. After 0.5 h, the solvent was evaporated *in vacuo* to yield an off-white solid. This was dissolved in dry dichloromethane (20 ml) and the solution was treated with dry triethylamine (2.0 ml, 0.0146 mol, 1.2 equiv.) dropwise *via* syringe, while stirring under nitrogen at room temperature. White fumes were liberated during the addition, and a white precipitate gradually appeared. After the addition was complete, the mixture was left to stir under nitrogen at room temperature for a further 16 h. More dichloromethane (10 ml) was added and the mixture washed with hydrochloric acid (2 M, 2 × 30 ml) and water (30 ml). The organic layer was dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a brown oil. This was purified by column chromatography (silica; 5% ethyl acetate in hexane elution) to yield (*E*)-3-bromo-4-phenylbut-3-en-2-one **19a** (2.518 g, 0.0112 mol, 92%) as a yellow oil, ν_{max}(film)/cm^{-1} 3073, 3026, 2933, 2855 (CH), 1679 (C=O), 1607, 1503, 1457 (CH), 757, 685, 612; δ_H(250 MHz, $CDCl_3$) 2.61 (3H, s, CH_3), 7.45 (3H, m, ArH), 7.87 (2H, m, ArH), 8.04 (1H, s, =CH); δ_C(67.8 MHz, $CDCl_3$) 27.1 (CH_3), 123.4 (C), 128.6 (CH), 130.6 (CH), 133.8 (C), 140.1 (CH), 193.2 (C=O); *m*/*z* 226 (M^+, 60%), 225 (60), 224 (M^+, 60), 223 (60), 145 (100), 102 (100).

3-Bromobut-3-en-2-one 19b.[20] [Prepared using same procedure as for **19a**] 3-Bromobut-3-en-2-one **19b** (4.158 g, 0.0279 mol, 98%) as a yellow oil, ν_{max}(film)/cm^{-1} 3011, 2917, 2854 (CH), 1703 (C=O), 1619 (C=C), 612 (C–Br); δ_H(270 MHz, $CDCl_3$) 2.47 (3H, s, CH_3), 6.43 (1H, d, *J* 2.4, =CH), 6.81 (1H, d, *J* 2.4, =CH); δ_C(67.8 MHz, $CDCl_3$) 26.1 (CH_3), 129.6 (CH_2), 132.0 (C), 192.0 (C=O).

Ethyl (E/Z)-2-bromobut-2-enoate 19c[21]

A solution of ethyl but-2-enoate **18c** (5.45 ml, 0.044 mol, 1.0 equiv.) in dry dichloromethane (40 ml) was treated dropwise with a solution of bromine (2.3 ml, 0.044 mol, 1.0 equiv.) in carbon tetrachloride (5 ml), whilst stirring under nitrogen at *ca.* −10 °C. The mixture was left to stir for 2 h before adding dry triethylamine (7.4 ml, 0.053 mol, 1.2 equiv.) dropwise *via* syringe, whilst cooling at 0 °C. This mixture was stirred for 1 h before washing with 2 M hydrochloric acid (3 × 50 ml). The combined aqueous layers were washed with dichloromethane (100 ml), and the combined organic layers were washed with water (50 ml), dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a dark oil. This was purified by column chromatography (silica; 5% ether in hexane elution) to afford ethyl (*E*/*Z*)-2-bromobut-2-enoate **19c** (8.494 g, 0.044 mol, 100%) as a yellow oil [Found: $(M + NH_4)^+$ (CI), 210.0130. $C_6H_9O_2Br$ requires $(M + NH_4)^+$, 210.0130]; ν_{max}(film)/cm^{-1} 2990, 2933 (CH), 1729 (C=O), 1635 (C=C), 1457 (CH), 1253, 1059 (C–O); δ_H(250 MHz, $CDCl_3$) 1.33, 1.35 (3H, 2 × t, *J* 7.1, CH_3), 1.95, 2.05 (3H, 2 × d, *J* 7.5, CH_3), 4.28 (2H, q, *J* 7.1, CH_2), 6.77, 7.39 (1H, 2 × q, *J* 7.5, =CH); δ_C(67.8 MHz, $CDCl_3$) 15.7 (CH_3), 15.8 (CH_3), 19.1 (CH_3), 19.5 (CH_3), 63.6 (CH_2), 63.9 (CH_2), 113.7 (C), 119.3 (C), 142.8 (CH), 145.0 (CH), 164.0 (C), 164.6 (C); *m*/*z* (CI) 212 [$(M + NH_4)^+$, 12%], 210 [$(M + NH_4)^+$, 12%], 164 (62), 148 (100).

2-Bromocyclopent-2-en-1-one 19d.[22] [Prepared using same procedure as for **19a**] 2-Bromocyclopent-2-en-1-one **19d** (4.99 g, 62%) as white needles, mp 37–38 °C (lit.,[22d] 39–39.5 °C); ν_{max}(KBr disc)/cm^{-1} 3055, 2921, 1708, 1663, 1584; δ_H($CDCl_3$, 250 MHz) 2.52–2.56 (2H, m, CH_2), 2.68–2.73 (2H, m, CH_2), 7.79 (1H, m, CH=); δ_C($CDCl_3$, 63 MHz) 28.0 (CH_2), 32.4 (CH_2), 125.9 (C), 162.1 (CH), 201.7 (C); *m*/*z* 162, 160 (M^+, 100%), 134, 132 (66), 84 (79).

2-Bromocyclohex-2-en-1-one 19e.[22a] [Prepared using same procedure as for **19a**] 2-Bromocyclohex-2-en-1-one **19e** (9.00 g, 51%) as white needles, mp 75–76 °C (lit.,[22a] 75–76 °C); ν_{max}(KBr disc)/cm^{-1} 2959, 2941, 2872, 1681, 1597; δ_H($CDCl_3$, 250 MHz) 2.08 (2H, m, CH_2), 2.46 (2H, m, CH_2), 2.64 (2H, t, *J* 6.5, CH_2),

7.44 (1H, t, *J* 4.0, =CH); δ_C($CDCl_3$, 63 MHz) 22.7 (CH_2), 28.4 (CH_2), 38.4 (CH_2), 123.7 (C), 151.5 (CH), 191.4 (C).

(*E*)-3-Bromo-4-phenylbut-3-en-2-ol 20a[11]

To a solution of cerium(III) chloride heptahydrate (2.481 g, 6.6 mmol, 1.0 equiv.) in methanol (20 ml) was added a solution of (*E*)-3-bromobut-3-en-2-one **19a** (1.50 g, 6.6 mmol, 1.0 equiv.) in methanol (10 ml). The mixture was stirred under nitrogen at 0 °C, and sodium borohydride (0.252 g, 6.6 mmol, 1.0 equiv.) was added a little at a time. Each addition was accompanied by a vigorous evolution of gas and an exotherm to *ca.* 15–20 °C. Once the addition was complete, the mixture was left to stir under nitrogen at this temperature for 2 h. Water (15 ml) was added and the mixture extracted with diethyl ether (3 × 30 ml). The combined organic layers were dried over anhydrous sodium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield (*E*)-3-bromo-4-phenylbut-3-en-2-ol **20a** (1.114 g, 4.9 mmol, 74%) as a pale yellow oil (Found: C, 53.0; H, 4.4. $C_{10}H_{11}BrO$ requires C, 52.9; H, 4.9%); ν_{max}(film)/cm^{-1} 3363 (OH), 3068, 3021, 2974, 2933, 2871 (CH), 1643, 1498 (C=C), 1452 (CH), 1084 (C–O), 763, 700 (Ar ring), 600; δ_H(270 MHz, $CDCl_3$) 1.48 (3H, d, *J* 6.2, CH_3), 2.03 (1H, br s, OH), 4.48 (1H, q, *J* 6.2, O-CH), 7.07 (1H, s, =CH), 7.34 (3H, m, ArH), 7.60 (2H, d, *J* 8.4, ArH); δ_C(67.8 MHz, $CDCl_3$) 22.8 (CH_3), 73.8 (CH), 127.2 (C), 128.4 (CH), 129.3, (CH), 131.6 (CH), 135.3 (C); *m*/*z* 228 (M^+, 17%), 226 (M^+, 21), 147 (92), 84 (100).

3-Bromobut-3-en-2-ol 20b. [Prepared using same procedure as for **20a**] 3-Bromobut-3-en-2-ol **20b** (1.855 g, 0.0123 mol, 61%) was obtained as a pale yellow oil, ν_{max}(film)/cm^{-1} 3373 (O–H), 2985 , 2938, 2886 (CH), 1638 (C=C), 1452 (CH), 1094 (C–O); δ_H(250 MHz, $CDCl_3$) 1.39 (3H, d, *J* 6.3, CH_3), 1.99 (1H, br s, OH), 4.33 (1H, q, *J* 6.4, O-CH), 5.53 (1H, d, *J* 2.0, =CH), 5.90 (1H, d, *J* 2.0, =CH); δ_C(67.8 MHz, $CDCl_3$) 23.7 (CH_3), 73.7 (CH), 117.4 (CH_2), 140.1 (C).

(*E*/*Z*)-2-Bromobut-2-en-1-ol 20c.[21] (*E*/*Z*)-2-Bromobut-2-en-1-ol **20c** (0.787 g, 5.2 mmol, 52%) as a pale yellow oil, ν_{max}(film)/cm^{-1} 3351 (OH), 2933, 2865 (CH), 1656 (C=C), 1441 (CH), 1242, 1054 (C–O); δ_H(250 MHz, $CDCl_3$) 1.77 (3H, m, CH_3), 2.11 (1H, br s, OH), 4.25, 4.32 (2H, 2 × s, CH_2), 6.08 (1H, q, *J* 7.2, =CH); δ_C(62.9 MHz, $CDCl_3$) 15.0 (CH_3), 16.3 (CH_3), 61.9 (CH_2), 67.9 (CH_2), 124.4 (C), 124.5 (CH), 127.6 (C), 129.8 (CH).

2-Bromocyclopent-2-en-1-ol 20d.[23] [Prepared using same procedure as for **20a**] 2-Bromocyclopent-2-en-1-ol **20d** (3.35 g, 76%) as a clear oil, ν_{max}(film)/cm^{-1} 3354, 3069, 2969, 2934, 2852, 1618; δ_H($CDCl_3$, 250 MHz) 1.83–1.88 (1H, m, CH_2), 2.22–2.43 (3H, m, CH_2), 2.82 (1H, br s, OH), 4.63–4.70 (1H, m, C*H*OH), 6.02 (1H, m, CH=); δ_C($CDCl_3$, 63 MHz) 30.4 (CH_2), 32.0 (CH_2), 79.3 (CH), 125.1 (C), 134.3 (CH); *m*/*z* (EI) 164, (M^+, 20%), 162 (M^+, 20), 86 (97), 84 (100), 83 (100).

2-Bromocyclohex-2-en-1-ol.[24] [Prepared using same procedure as for **20a**] 2-Bromocyclohex-2-en-1-ol **20e** (6.44 g, 73%) as a yellow oil, ν_{max}(film)/cm^{-1} 3364, 2945, 2862, 2836, 1641; δ_H($CDCl_3$, 250 MHz) 1.65–2.12 (6H, m, $3CH_2$), 2.10 (1H, s, OH), 4.19 (1H, t, *J* 4.7, C*H*OH), 6.20 (1H, t, *J* 4.0, CH=); δ_C($CDCl_3$, 63 MHz) 17.6 (CH_2), 27.8 (CH_2), 32.2 (CH_2), 70.2 (CH), 125.7 (C), 132.8 (CH); *m*/*z* (EI) 178, 176 $(M - H)^+$ (25%), 150, 148 (85), 97 (100), 79 (100).

2-Bromocyclonon-2-enol 20f. [Prepared as in ref. 16] 2-Bromocyclonon-2-enol **20f** (2.13 g, 82%) as a clear oil and as an 11:9:2 mixture of the 2 *Z* rotamers and the *E* isomer, ν_{max}(film)/cm^{-1} 3357, 2939, 2861, 1639; δ_H($CDCl_3$, 250 MHz) 0.88–2.51 (13H, m, 6 CH_2, OH), 4.00 ($1H^Z$ minor, dd, *J* 10.5, 4.3, C*H*OH^Z minor), 4.49–4.53 ($1H^E$, m, C*H*OH^E), 4.71 ($1H^Z$ major; dd, *J* 7.5, 7.5, C*H*OH^Z major), 6.01 ($1H^Z$ minor, dd, *J* 10.3, 5.3, CH=^{Z} minor), 6.17 ($1H^Z$ major, dd, *J* 9.0, 9.0, CH=^{Z} major), 6.37 ($1H^E$, dd, *J* 5.5, 10.5, CH=^{E}); δ_C($CDCl_3$, 63 MHz) 22.7 (CH_2), 23.0 (CH_2), 24.7 (CH_2), 24.8 (CH_2), 25.8 (CH_2), 26.7 (CH_2), 27.1 (CH_2), 27.3 (CH_2), 28.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.4 (CH_2), 33.6 (CH_2), 35.0 (CH_2), 35.7 (CH_2), 69.5 (CH), 75.6 (CH), 77.1 (CH), 127.9 (CH), 128.2 (CH), 130.9 (C), 132.3 (C), 133.3 (CH); *m*/*z* 220 (M^+, 46%), 218 (M^+, 46), 150 (100), 148 (100).

***N*-(2-Nitrophenyl)methanesulfonamide 21**[25]

To a solution of 2-nitroaniline (276.25 g, 2.0 mol, 1.0 equiv.) and 4-dimethylaminopyridine (24.00 g, 0.2 mol, 0.1 equiv.) in pyridine (690 ml) was added methanesulfonyl chloride (185 ml, 2.4 mol, 1.2 equiv.) slowly. After heating at reflux for 18 h, the solution was allowed to cool before diluting with dichloromethane (1500 ml). The mixture was washed with 2 M hydrochloric acid (4 × 600 ml). The combined aqueous layers were cooled to 0 °C and acidified to pH 6 using concentrated hydrochloric acid. A dense precipitate appeared. The mixture was then extracted with dichloromethane (3 × 600 ml). The combined organic layers were washed with water (2 × 800 ml), dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo*. The residual solid was recrystallised from ethyl acetate to yield *N*-(2-nitrophenyl)methanesulfonamide **21** (183.45 g, 0.9959 mol, 50%) as a yellow crystalline solid, mp 101–103 °C (Found: C, 39.0; H, 3.8; N, 12.8. M^+, 216.0203. $C_7H_8N_2O_4S$ requires C, 38.9; H, 3.7; N, 13.0%. M^+ 216.0205); ν_{max}(KBr disc)/cm^{-1} 3266, 1615, 1578; δ_H($CDCl_3$, 400 MHz) 3.17 (3H, s, SO_2CH_3), 7.23 (1H, ddd, *J* 8.4, 8.4, 1.0, ArH), 7.68 (1H, ddd, *J* 8.5, 8.5, 1.0, ArH), 7.86 (1H, dd, *J* 8.4, 1.0, ArH), 8.23 (1H, dd, *J* 8.5, 1.0, ArH), 9.70 (1H, br s, NH); δ_C($CDCl_3$, 100 MHz) 41.1 (CH_3), 119.9 (CH), 124.0 (CH), 127.0 (CH), 134.7 (C × 2), 136.8 (CH); *m*/*z* (EI^+) 216 (M^+, 62%), 138 (100), 108 (36), 91 (22).

***N*-(2-Bromo-1-methyl-3-phenylprop-2-enyl)-*N*-(2-nitrophenyl)-methanesulfonamide 22a and *N*-(2-bromo-1-phenylbut-2-enyl)-*N*-(2-nitrophenyl)methanesulfonamide 22a′**

To a solution of (*E*)-3-bromo-4-phenylbut-3-en-2-ol **20a** (1.0 g, 4.4 mmol, 1.0 equiv.), *N*-(2-nitrophenyl)methanesulfonamide **21** (0.952 g, 4.4 mmol, 1.0 equiv.) and triphenylphosphine (1.616 g, 6.2 mmol, 1.4 equiv.) in dry tetrahydrofuran (10 ml) was added a solution of diethyl azodicarboxylate (1.0 ml, 6.2 mmol, 1.4 equiv.) in dry tetrahydrofuran (2 ml) dropwise *via* syringe whilst stirring under nitrogen at 0 °C. Once the addition was complete, the mixture was left to stir under nitrogen at room temperature for 20 h. Water (10 ml) was added to quench the reaction and the mixture evaporated to dryness *in vacuo*. The residue was partitioned between water (25 ml) and ethyl acetate (25 ml). The aqueous phase was washed with more ethyl acetate (2 × 25 ml). The combined organic layers were washed sequentially with 2 M sodium hydroxide solution (25 ml) and water (25 ml), dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a yellow oil–white solid mixture. This was purified by column chromatography (silica; 45% dichloromethane in hexane to 100% dichloromethane gradient elution) to yield *N-(2-bromo-1-methyl-3-phenylprop-2-enyl)-N-(2-nitrophenyl)methanesulfonamide* **22a** and *N-(2-bromo-1-phenylbut-2-enyl)-N-(2-nitrophenyl)-methanesulfonamide* **22a′** (1.248 g, 3.0 mmol, 67%) as an inseparable mixture and as a sticky yellow oil [Found: M^+ (EI), 426.0065. $C_{17}H_{17}{}^{81}BrN_2O_4S$ requires *M*, 426.0072]; ν_{max}(film)/cm^{-1} 3062, 3026, 2990, 2933, 2876 (CH), 1602 (C=C), 1540 (ON=O), 1486, 1446 (CH), 1371 (ON=O), 1348, 1161 (N–SO_2), 778, 700 (Ar ring), 607 (C–Br); δ_H(400 MHz, $CDCl_3$) 1.26 (*J* 6.8), 1.51 (*J* 6.8), 1.74 (*J* 6.0) and 1.75 (*J* 6.0) (4 × d, CH_3), 2.97, 2.99, 3.03 and 3.35 (3H, 4 × s, CH_3), 5.04 (1H, *J* 6.8), 5.34 (1H, *J* 6.8), 6.42 (1H, *J* 6.0), 6.54 (1H, *J* 6.0), (4 × q, N-CH),

5.96, 6.07, 6.77 (3 × s, =CH), 7.19–8.07 (10H, m, =CH, ArH); δ_C(62.9 MHz, $CDCl_3$) 14.0 (CH_3), 16.7 (CH_3), 19.5 (CH_3), 20.2 (CH_3), 41.7 (CH_3), 42.6 (CH_3), 63.7 (CH), 65.4 (CH), 72.1 (CH), 72.7 (CH), 124.4 (C), 124.8 (CH), 124.9 (CH), 125.4 (CH), 125.6 (CH), 126.9 (C), 127.6 (C), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 128.5 (CH), 128.9 (CH), 129.0 (CH), 129.3 (CH), 129.4 (CH), 129.5 (CH), 129.9 (CH), 130.0 (CH), 130.1 (CH), 130.6 (C), 131.5 (CH), 132.0 (C), 132.2 (C), 132.3 (CH), 132.4 (CH), 132.6 (CH), 133.1 (CH), 133.2 (CH), 133.4 (CH), 134.5 (C), 134.5 (CH), 134.6 (CH), 134.9 (C), 135.2 (CH), 135.7 (CH), 136.1 (C), 149.9 (C); *m*/*z* (EI) 426 (M^+, 5%), 424 (M^+, 6), 345 (48), 129 (86), 79 (100).

***N*-(2-Bromo-1-methylprop-2-enyl)-*N*-(2-nitrophenyl)methanesulfonamide 22b.** [Prepared using same procedure as for **22a**] *N-(2-Bromo-1-methylprop-2-enyl)-N-(2-nitrophenyl)methanesulfonamide* **22b** (1.315 g, 3.9 mmol, 78%) as a pale yellow solid, mp 92.5–94 °C (Found: C, 37.9; H, 3.7; N, 7.8. $C_{11}H_{13}BrN_2O_4S$ requires C, 37.8; H, 3.8; N, 8.0%) [Found: $(M + NH_4)^+$ (CI), 366.0123. $C_{11}H_{13}BrN_2O_4S$ requires $(M + NH_4)^+$, 366.0123]; ν_{max}(KBr disc)/cm^{-1} 3109, 3071, 2990, 2938, 2876 (CH), 1625, 1601 (C=C), 1540 (ON=O), 1483, 1450 (CH), 1371 (ON=O), 1348, 1161 (N–SO_2), 773 (Ar ring), 621 (C–Br); NMR spectra show a mixture of rotamers—the chemical shifts of the *major* rotamer are reported here. δ_H(270 MHz, $CDCl_3$) 1.16 (3H, d, *J* 6.8, CH_3), 3.01 (3H, s, CH_3), 5.16 (1H, q, *J* 6.8, N-CH), 5.77 (1H, d, *J* 2.2, =CH), 6.15 (1H, d, *J* 2.0, =CH), 6.49 (2H, d, *J* 2.0, =CH), 7.58 (1H, dd, *J* 7.7, 7.7, ArH), 7.68 (1H, ddd, *J* 7.7, 7.7, 1.6, ArH), 7.87 (1H, dd, *J* 7.7, 1.6, ArH), 8.02 (1H, dd, *J* 7.7, 1.6, ArH); δ_C(67.8 MHz, $CDCl_3$) 19.4 (CH_3), 42.0 (CH_3), 62.4 (CH), 122.3 (C), 122.7 (CH_2), 126.0 (CH), 130.4 (CH), 130.6 (C), 133.7 (CH), 134.8 (C), 134.9 (CH); *m*/*z* (CI) 366 [$(M + NH_4)^+$, 100%], 321 (68), 319 (70), 239 (40).

***N*-[(*E*/*Z*)-2-Bromobut-2-enyl]-*N*-(2-nitrophenyl)methanesulfonamide 22c.** [Prepared using same procedure as for **22a**] *N-[(E/Z)-2-Bromobut-2-enyl]-N-(2-nitrophenyl)methanesulfonamide* **22c** (0.954 g, 2.7 mmol, 83%) as a yellow oil [Found (CI): $(M + NH_4)^+$ 366.0123. $C_{11}H_{13}BrN_2O_4S$ requires $(M + NH_4)^+$, 366.0123]; ν_{max}(film)/cm^{-1} 3079, 3037, 3011, 2943, 2886, 2859 (CH), 1609 (C=C), 1541 (ON=O), 1488, 1457 (CH), 1352 (ON=O, N–SO_2), 1169 (N–SO_2), 777 (Ar ring); δ_H(250 MHz, $CDCl_3$) 1.41, 1.70 (3H, 2 × d, *J* 7.3, CH_3), 3.12, 3.15 (3H, 2 × s, CH_3), 4.62, 4.80 (2H, 2 × m, CH_2), 5.88, 6.12 (1H, 2 × q, *J* 7.3, =CH), 7.60 (3H, m, ArH), 7.97 (1H, m, ArH); δ_C(62.9 MHz, $CDCl_3$) 15.3, 17.3 (CH_3), 41.8 (CH_3), 41.8 (CH_3), 54.5 (CH_2), 60.8 (CH_2), 119.0 (C), 122.8 (C), 126.0 (CH), 126.1 (CH), 130.3 (CH), 130.5, (CH), 131.7 (CH), 132.1 (C), 132.2 (C), 134.0 (CH), 134.6 (CH), 134.7 (CH), 135.1 (CH), 149.1 (C), 149.4 (C); *m*/*z* 368 ($M + NH_4^+$, 90%), 366 ($M + NH_4^+$, 90), 321 (100), 319 (100), 241 (37), 239 (36).

***N*-(2-Bromocyclopent-2-en-1-yl)-*N*-(2-nitrophenyl)methanesulfonamide 22d.** [Prepared using same procedure as for **22a**] *N-(2-Bromocyclopent-2-en-1-yl)-N-(2-nitrophenyl)methanesulfonamide* **22d** (4.39 g, 61%) as a 2:1 mixture of rotamers by ^{1}H NMR, and as off-white needles, mp 148–149 °C (Found: C, 40.1; H, 3.5, N, 7.7. $C_{12}H_{13}BrN_2O_4S$ requires C, 39.9; H, 3.6; N, 7.8%); ν_{max}(KBr disc)/cm^{-1} 2932, 2865, 1602, 1583, 1536, 1481, 1341, 1150; δ_H($CDCl_3$, 250 MHz) 1.81–1.88 (1H major, m, CH_2 major), 2.04–2.18 (2H, m, CH_2), 2.42–2.54 (1H major + 2H minor, m, CH_2), 3.18 (3H major, s, SO_2CH_3), 3.21 (3H minor, s, SO_2CH_3), 4.78–4.84 (1H minor, br m, CHN), 5.48–5.53 (1H major, m, CHN), 6.15–6.16 (1H, m, CH=), 7.53–7.68 (2H major + 4H minor, m, ArH), 7.85 (1H major, dd, *J* 8.2, 8.2, ArH), 7.99 (1H major, d, *J* 7.3, ArH); δ_C($CDCl_3$, 63 MHz) 28.0 (CH_2), 29.8 (CH_2 minor), 30.3 (CH_2), 30.8 (CH_2 minor), 41.6 (CH_3 minor), 41.8 (CH_3), 70.4 (CH), 73.8 (CH minor), 118.7 (C minor), 121.3 (C), 125.1 (CH minor), 126.1 (CH), 128.8 (C), 129.9 (CH minor), 130.2 (CH), 132.2 (C minor), 133.2 (CH), 133.3 (CH minor), 133.6 (CH), 134.4 (CH minor), 139.0 (CH), 139.7 (CH minor), 149.7 (C); *m*/*z* (EI) 362 (M^+, 1%), 360 (M^+, 1%), 283 (100), 281 (100).

***N*-(2-Bromocyclohex-2-en-1-yl)-*N*-(2-nitrophenyl)methanesulfonamide 22e.** [Prepared using same procedure as for **22a**] *N-(2-Bromocyclohex-2-en-1-yl)N-(2-nitrophenyl)-methanesulfonamide* **22e** (3.54 g, 56%), as a 7:1 mixture of rotamers by ^{1}H NMR, and as off-white needles, mp 152–153 °C [Found: C, 41.68; H, 4.08, N, 7.47. $C_{13}H_{15}BrN_2O_4S$ requires C, 41.61; H, 4.03; N, 7.47%] [Found (CI): $(M + NH_4)^+$ 392.0285. $C_{11}H_{15}BrN_2O_4S$ requires $(M + NH_4)^+$, 392.0280]; ν_{max}(KBr disc)/cm^{-1} 1600, 1543, 1362, 1341, 1150; δ_H($CDCl_3$, 250 MHz) 1.08–2.70 (6H, br m, CH_2), 3.16 (3H major, br s, SO_2CH_3 major), 3.38 (3H minor, br s, SO_2CH_3 minor), 4.75–5.02 (1H, br m, CHN), 6.35–6.42 (1H, br m, CH=), 7.50–7.65 (2H, m, ArH), 7.76–7.79 (1H, m, ArH), 7.96–7.99 (1H, m, ArH); δ_C($CDCl_3$, 63 MHz) 17.4 (CH_2), 27.4 (CH_2), 31.3 (CH_2), 40.6 (CH), 63.0 (CH_3), 121.0 (C), 126.2 (CH), 129.9 (CH), 130.2 (C), 132.9 (CH), 133.4 (CH), 138.8 (CH), 150.0 (C); *m*/*z* (CI) 394 [$(M + NH_4)^+$, 60%], 392 [$(M + NH_4)^+$, 55], 347 (100), 345 (86), 269(35), 267 (53), 265 (64).

***N*-[(*Z*)-2-Bromocyclonon-2-enyl]-*N*-(2-nitrophenyl)methanesulfonamide 22f**

2-Nitro-*N*-methylsulfonylaniline **21** (2.59 g, 12 mmol, 1.5 equiv.) and methyldiphenylphosphine (2.40 g, 12 mmol, 1.5 equiv.) were stirred in tetrahydrofuran (50 ml) under nitrogen at 0 °C. 2-Bromocyclonon-2-enol[16] **20f** (1.75 g, 8 mmol, 1 equiv.) was added, followed by diethyl azodicarboxylate (2.09 g, 12 mmol, 1.5 equiv.), and the solution was allowed to warm to room temperature and stir for 30 min. The mixture was then heated under reflux and stirred for 48 h. The solvent was removed *in vacuo* and the resultant oil was dissolved in ethyl acetate (20 ml) and washed with sodium hydroxide (2 M, 3 × 20 ml), hydrochloric acid (2 M, 20 ml), and brine (20 ml). The solution was dried over magnesium sulfate and the solvent removed *in vacuo* to give a brown solid (4.0 g). Initial gradient elution column chromatography using ~15 g of silica and 50% dichloromethane–50% hexane to 100% dichloromethane removed the bulk of triphenylphosphine oxide and reduced DEAD impurities. Further purification using ~6 g of silica and 50% diethyl ether–50% hexane to 100% diethyl ether gave the *trans* diastereomer, present in only one rotameric form, *N-[(Z)-2-bromocyclonon-2-enyl]-N-(2-nitrophenyl)methanesulfonamide* **22f** (1.38 g, 41.2%) as yellow crystals, mp 167 °C (Found: C, 45.9; H, 4.9, N, 6.59. $C_{16}H_{21}BrN_2O_4S$ requires C, 46.1; H, 5.1; N, 6.7%); ν_{max}(KBr disc)/cm^{-1} 2929, 2919, 2906, 1602, 1540, 1355, 1340, 1154; δ_H($CDCl_3$, 250 MHz) 1.15–1.72 (8H, m, 4CH_2), 1.78–2.09 (2H, m, CH_2), 2.24–2.52 (2H, m, CH_2), 3.02 (3H, s, SO_2CH_3), 5.59 (1H, dd, *J* 4.5, 12.0, CHN), 6.46 (1H, dd, *J* 8.9, 8.9, CH=), 7.56–7.76 (2H, m, ArH), 7.88 (1H, dd, *J* 7.7, 1.3, ArH), 8.05 (1H, dd, *J* 7.7, 1.5, ArH); δ_C($CDCl_3$, 63 MHz) 22.2 (CH_2), 26.1 (CH_2), 27.8 (CH_2), 28.9 (CH_2), 30.6 (CH_2), 30.6 (CH_2), 42.2 (CH_3), 60.4 (CH), 125.9 (CH), 127.0 (C), 130.2 (CH), 131.1 (C), 133.7 (CH), 134.9 (CH), 138.6 (CH), 150.3 (C); *m*/*z* (EI) 418 (M^+, 8%), 416 (M^+, 7), 337 (100), 258 (22), 257 (22).

***N*-(2-Aminophenyl)-*N*-[(*E*)-2-bromo-1-methyl-3-phenylprop-2-enyl]methanesulfonamide 23a**

A mixture of sodium borohydride (0.182 g, 4.8 mmol, 1.0 equiv.) and copper(II) acetylacetonate (0.254 g, 1.0 mmol, 0.2 equiv.) in ethanol (130 ml) was stirred under nitrogen at room temperature until a black suspension formed in a clear solution. Sodium borohydride (0.363 g, 9.6 mmol, 2.0 equiv.) was added, followed by a solution of *N*-[(*E*)-2-bromo-1-methyl-3-phenylprop-2-enyl]-*N*-(2-nitrophenyl)methanesulfonamide **22a** (2.0 g, 4.8 mmol, 1.0 equiv.) in ethanol (130 ml), and the resultant

mixture stirred under nitrogen at room temperature overnight. Water (200 ml) was added to quench the reaction, and the mixture filtered through kieselguhr before evaporating to dryness *in vacuo*. The residue was partitioned between water (100 ml) and dichloromethane (100 ml). The aqueous layer was washed with more dichloromethane (100 ml), and the combined organic layers washed with water (100 ml). The organic phase was dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a yellow oil. This was purified by column chromatography (silica; 100% dichloromethane elution) to yield *N-(2-aminophenyl)-N-[(E)-2-bromo-1-methyl-3-phenylprop-2-enyl]methanesulfonamide* **23a** (1.55 g, 4.0 mmol, 84%) as a pale yellow solid, mp 136–137.5 °C (Found: C, 51.5; H, 4.8; N, 6.9. $C_{17}H_{19}BrN_2O_2S$ requires C, 51.7; H, 4.8; N, 7.1%) [Found: M^+ (EI), 394.0354. $C_{17}H_{19}BrN_2O_2S$ requires *M*, 394.0351]; ν_{max}(KBr disc)/cm^{-1} 3472, 3383 (NH_2), 3063, 3027, 2953, 2927, 2880 (CH), 1619, 1504 (C=C), 1447 (CH), 1316, 1154 (N–SO_2), 761 (Ar ring). NMR spectra showed a mixture of rotamers—the chemical shifts of the protons of the *major* rotamer are reported here. δ_H(270 MHz, $CDCl_3$) 1.44 (3H, d, *J* 7.0, CH_3), 3.09 (3H, s, CH_3), 4.16 (2H, br s, NH_2), 5.35 (1H, q, *J* 7.0, N–CH), 6.70–6.88 (3H, m, ArH + =CH), 7.17–7.49 (7H, m, ArH); δ_C(67.8 MHz, $CDCl_3$) 19.6 (CH_3), 40.2 (CH_3), 64.2 (CH), 117.4 (CH), 118.2 (CH), 121.1 (C), 126.8 (C), 128.3 (CH), 128.5 (CH), 129.1 (CH), 130.5 (CH), 132.3 (CH), 133.0 (CH), 135.2 (C), 148.5 (C).

***N*-(2-Aminophenyl)-*N*-(2-bromo-1-methylprop-2-enyl)-methanesulfonamide 23b.** [Prepared using same procedure as for **23a**] *N-(2-Aminophenyl)-N-(2-bromo-1-methylprop-2-enyl)-methanesulfonamide* **23b** (0.217 g, 0.7 mmol, 78%) as a pale yellow solid, mp 113–114 °C [Found: M^+ (EI), 318.0055. $C_{11}H_{15}BrN_2O_2S$ requires *M*, 318.0038]; ν_{max}(KBr disc)/cm^{-1} 3451, 3371 (NH_2), 3074, 3037, 2990, 2927, 1621 (C=C), 1497, 1454 (CH), 1321, 1154 (N–SO_2), 762; NMR spectra show a mixture of rotamers—the chemical shifts of the *major* rotamer are reported here. δ_H(400 MHz, $CDCl_3$) 1.35 (3H, d, *J* 7.0, CH_3), 3.15 (3H, s, CH_3), 3.90 (2H, br s, NH_2), 5.19 (1H, q, *J* 7.0, N-CH), 5.69 (1H, d, *J* 2.3, =CH), 5.78 (1H, d, *J* 2.2, =CH), 6.72 (1H, ddd, *J* 7.8, 7.8, 1.3, ArH), 6.80 (1H, dd, *J* 8.0, 1.3, ArH), 7.18 (1H, ddd, *J* 8.0, 8.0, 1.5, ArH), 7.32 (1H, dd, *J* 8.0, 1.5, ArH); δ_C(100.6 MHz, $CDCl_3$) 19.1 (CH_3), 40.1 (CH_3), 62.7 (CH), 117.6 (CH), 118.5 (CH), 121.0 (C), 121.8 (CH_2), 130.6 (CH), 132.9 (CH), 134.0 (C), 148.5 (C); *m/z* 320 (M^+, 28%), 318 (M^+, 29), 241 (62), 239 (100), 185 (34), 159 (73).

***N*-(2-Aminophenyl)-*N*-[(*E*/*Z*)-2-bromobut-2-enyl]methanesulfonamide 23c.** [Prepared using same procedure as for **23a**] *N-(2-Aminophenyl)-N-[(E/Z)-2-bromobut-2-enyl]methanesulfonamide* **23c** (0.204 g, 0.6 mmol, 58%) as a pale yellow oil (Found: C, 41.7; H, 4.9; N, 8.5. $C_{11}H_{15}BrN_2O_2S$ requires C, 41.4; H, 4.7; N, 8.8%) [Found: $(M + H)^+$ (CI), 319.0116. $C_{11}H_{15}BrN_2O_2S$ requires $(M + H)^+$, 319.0116]; ν_{max}(film)/cm^{-1} 3482, 3383 (NH_2), 3032, 2927, 2854 (CH), 1619, 1504 (C=C), 1462 (CH), 1326, 1159 (N–SO_2), 761 (Ar ring); δ_H(400 MHz, $CDCl_3$) 1.26, 1.66 (3H, 2 × d, *J* 7.3, CH_3), 3.12, 3.17 (3H, 2 × s, CH_3), 4.03 (2H, br s, NH_2), 4.55 (2H, s + br m, CH_2), 5.75, 6.04 (1H, 2 × q, *J* 7.3, =CH), 6.75 (2H, m, ArH), 7.15 (2H, m, ArH); δ_C(100.6 MHz, $CDCl_3$) 14.6, 17.0, 39.7, 40.1 (CH_3), 51.9, 58.9 (CH_2), 117.2 (CH), 117.4 (CH), 118.7 (CH), 118.7 (CH), 119.1 (C), 122.9 (C), 123.6 (C), 123.8 (C), 130.2 (CH), 130.2 (CH), 130.3, (CH), 130.5 (CH), 134.1 (CH), 146.5 (C), 146.5 (C); *m/z* 321, 319 [$(M + H)^+$, 14%], 159 (77), 133 (74), 119 (100), 109 (72).

***N*-(2-Aminophenyl)-*N*-(2-bromocyclopent-2-en-1-yl)methanesulfonamide 23d.** [Prepared using same procedure as for **23a**] *N-(2-Aminophenyl)-N-(2-bromocyclopent-2-en-1-yl)methanesulfonamide* **23d** (1.19 g, 90%) as an 8 : 1 mixture of rotamers by ^{1}H NMR, and as off-white needles, mp 149–150 °C [Found: C, 43.34; H, 4.40, N, 8.21. $C_{12}H_{15}BrN_2O_2S$ requires C, 43.51; H, 4.56; N, 8.46%] [Found: M^+, 331.9967. $C_{12}H_{15}{}^{81}BrN_2O_2S$ requires *M*, 331.9987. Found: M^+, 330.0021. $C_{12}H_{15}{}^{79}BrN_2O_2S$ requires *M*, 330.0038]; ν_{max}(KBr disc)/cm^{-1} 3460, 3371, 2964, 2932, 2917, 1624, 1498; δ_H($CDCl_3$, 250 MHz) 1.55–1.62 (1H, m, CH_2), 1.93–2.06 (1H, m, CH_2), 2.06–2.41 (2H, m, CH_2), 3.10 (3H minor, s, SO_2CH_3), 3.22 (3H major, m, SO_2CH_3), 3.52–4.31 (2H, br s, NH_2), 5.02–5.09 (1H minor, m, CHN), 5.43–5.47 (1H major, m, CHN), 6.02–6.08 (1H, m, CH=), 6.71 (1H, dd, *J* 7.3, 7.3, ArH), 6.80 (1H, d, *J* 7.5, ArH), 7.15–7.21 (2H, m, ArH); δ_C($CDCl_3$, 63 MHz) 28.2 (CH_2), 30.7 (CH_2), 40.3 (CH_3), 70.3 (CH), 117.8 (CH), 118.6 (CH), 121.1 (C), 121.2 (C), 130.5 (CH), 132.1 (CH), 138.7 (CH), 147.9 (C); *m/z* (EI^+) 332 (M^+, 33%), 330 (M^+, 28), 253 (41), 251 (42), 186 (100), 107 (100).

***N*-(2-Aminophenyl)-*N*-(2-bromocyclohex-2-en-1-yl)methanesulfonamide 23e.** [Prepared using same procedure as for **23a**] *N-(2-Aminophenyl)-N-(2-bromocyclohex-2-en-1-yl)methanesulfonamide* **23e** (1.34 g, 93%), as a 4 : 1 mixture of rotamers by ^{1}H NMR, and as off-white needles, mp 129–131 °C (Found: C, 45.35; H, 4.93, N, 7.93. $C_{13}H_{17}BrN_2O_2S$ requires C, 45.23; H, 4.96; N, 8.11%); ν_{max}(KBr disc)/cm^{-1} 3472, 3430, 3384, 3358, 3316, 3011, 3037, 2933, 2902, 2866, 2829, 1628, 1597, 1312, 1146; δ_H($CDCl_3$, 250 MHz) 1.05–1.20 (1H, m, CH_2), 1.42–1.53 (1H, m, CH_2), 1.82–2.14 (3H, m, CH_2), 2.26–2.38 (1H, m, CH_2), 3.19 (3H minor, s, SO_2CH_3 minor), 3.21 (3H major, s, SO_2CH_3 major), 4.38 (2H, br s, NH_2), 5.07 (1H, br t, CHN), 6.32 (1H, t, *J* 4.2, CH=), 6.76–6.92 (2H major + 1H minor, m, 2ArH major, 1ArH minor), 7.17 (1H major, ddd, *J* 7.8, 7.8 1.6, ArH major), 7.33–7.37 (1H major + 3H minor, m, ArH major, 3ArH minor); δ_C($CDCl_3$, 63 MHz) 17.5 (CH_2 minor), 17.6 (CH_2), 27.0 (CH_2 minor), 27.1 (CH_2), 31.1 (CH_2 minor), 31.8 (CH_2), 38.9 (CH_3), 40.4 (CH_3 minor), 61.4 (CH minor), 61.6 (CH), 116.1 (CH minor), 117.4 (CH), 118.3 (CH), 121.1 (C minor), 121.7 (C minor), 121.8 (C), 122.1 (C), 130.2 (CH), 130.3 (CH minor), 131.0 (CH minor), 131.7 (CH), 137.0 (CH), 137.3 (CH minor), 148.2 (C), 151.3 (C minor); *m/z* (ES^+) 347 (MH^+, 93%), 345 (MH^+, 100), 187 (38).

Some separation of these rotameric diastereomers was possible by column chromatography, and as a result the ^{1}H NMR spectrum of the major diastereomer was obtained. The separated diastereomers quickly became a mixture again at room temperature. Major rotameric diastereomer: δ_H($CDCl_3$, 250 MHz) 1.05–1.20 (1H, m, CH_2), 1.42–1.53 (1H, m, CH_2), 1.82–2.14 (3H, m, CH_2), 2.26–2.38 (1H, m, CH), 3.21 (3H, s, CH_3), 4.38 (2H, br s, NH_2), 5.07 (1H, br t, CHN), 6.32 (1H, t, *J* 4.2, CH=), 6.69–6.80 (2H, m, ArH), 7.17 (1H, ddd, *J* 7.8, 7.8 1.6, ArH), 7.35 (1H, dd, *J* 7.9, 1.5, ArH).

***N*-(2-Aminophenyl)-*N*-(2-bromocyclonon-2-enyl)methanesulfonamide 23f.** [Prepared using same procedure as for **23a**] *N-(2-Aminophenyl)-N-(2-bromocyclonon-2-enyl)methanesulfonamide* **23f** (428 mg, 73.7%), as a complicated mixture of rotamers by ^{1}H NMR, and as a yellow oil [Found: M^+, 388.0652. $C_{16}H_{23}{}^{81}BrN_2O_2S$ requires *M*, 388.0613] [Found: M^+, 386.0611. $C_{16}H_{23}{}^{79}BrN_2O_2S$ requires *M*, 386.0664]; ν_{max}(KBr disc)/cm^{-1} 3454, 3366, 2929, 2859, 1623, 1334, 1153; δ_H($CDCl_3$, 250 MHz) 1.13–2.41 (12H, m, CH_2), 2.95, 3.00, 3.13 (3H, 3 × s, SO_2CH_3), 3.69–4.39 (2H, br s, NH_2), 5.19–6.42 (2H, m, CHN, CH=), 6.70–6.82 (2H, m, Ar), 7.08–7.55 (2H, m, ArH); δ_C($CDCl_3$, 63 MHz) 22.8 (CH_2), 23.1 (CH_2), 25.6 (CH_2), 25.8 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 26.8 (CH_2), 27.1 (CH_2), 27.4 (CH_2), 27.6 (CH_2), 27.7 (CH_2), 28.3 (CH_2), 28.5 (CH_2), 29.9 (CH_2), 31.2 (CH_2), 33.6 (CH_2), 39.1 (CH_3), 40. 5 (CH_3), 40.7 (CH_3), 57.2 (CH), 57.7 (CH), 116.5 (CH), 116.8 (CH), 117.6 (CH), 117.7 (CH), 117.9 (CH), 118.1 (CH), 121.5 (C), 121.8 (C), 122.4 (C), 127.4 (CH), 128.3 (CH), 129.9 (CH), 130.0 (CH), 130.5 (CH), 131.8 (CH), 132.2 (CH), 132.8 (CH), 133.1 (CH), 147.6 (C), 148.3 (C), 148.4 (C); *m/z* (EI) 388 (M^+, 6%), 386

(M^+, 6), 309 (49), 307 (57), 229 (60), 227 (51), 186 (71), 119 (76), 107 (100).

3-Benzyl-2-methyl-1-(methylsulfonyl)-1*H*-indole 24a

A suspension of nitrosonium tetrafluoroborate (0.037 g, 0.3 mmol, 1.2 equiv.) in dry dichloromethane (3 ml) was treated dropwise with a solution of *N*-(2-aminophenyl)-*N*-[(*E*)-2-bromo-1-methyl-3-phenylprop-2-enyl]methanesulfonamide **23a** (0.103 g, 0.3 mmol, 1.0 equiv.) in dry dichloromethane (1 ml) whilst stirring under nitrogen at room temperature. A dark red–brown coloured solution formed. The mixture was stirred at room temperature for 3.5 h before evaporating the solvent *in vacuo* to yield a red–brown oil. This was dissolved in degassed AR acetone (3 ml), and stirred under nitrogen at room temperature. Sodium iodide (0.040 g, 0.3 mmol, 1.0 equiv.) was added in one portion. A vigorous evolution of gas was observed, along with a colour change to dark brown. The resultant mixture was left to stir under nitrogen for 16 h. The solvent was evaporated *in vacuo* to yield a dark solid which was partitioned between dichloromethane (10 ml) and water (10 ml). The organic phase was washed with sodium thiosulfate solution (10 ml) and brine (10 ml). The combined organic layers were dried over anhydrous magnesium sulfate, filtered through kieselguhr and evaporated *in vacuo* to yield a brown solid. This was purified by column chromatography (silica; 20% ethyl acetate in hexane elution) to yield *3-benzyl-2-methyl-1-(methylsulfonyl)-1H-indole* **24a** (0.039 g, 0.1 mmol, 49%) as a pale yellow solid, mp 81.5–83 °C [Found: M^+ (EI), 299.0966. $C_{17}H_{17}NO_2S$ requires *M*, 299.0980]; ν_{max}(KBr disc)/cm^{-1} 3062, 3032, 2938, 2857 (CH), 1604 (C=C), 1498, 1457 (CH), 1363, 1180 (N–SO_2), 772 (Ar ring); δ_H(400 MHz, $CDCl_3$) 2.60 (3H, s, CH_3), 3.03 (3H, s, CH_3), 4.07 (2H, s, CH_2), 7.24 (7H, m, ArH) 7.39 (1H, dd, *J* 7.8, 1.0, ArH), 8.03 (1H, dd, *J* 8.0, 1.1, ArH); δ_C(100.6 MHz, $CDCl_3$) 13.0 (CH_3), 30.2 (CH_2), 40.7 (CH_3), 114.3 (CH), 119.1 (C), 119.2 (CH), 123.8 (CH), 124.4 (CH), 126.5 (CH), 128.3 (CH), 128.8 (CH), 130.8 (C), 133.8 (C), 136.4 (C), 139.7 (C); *m*/*z* (EI) 299 (M^+, 40%), 220 (70), 153 (100), 136 (79), 107 (66).

2,3-Dimethyl-1-(methylsulfonyl)-1*H*-indole 24b. [Prepared using same procedure as for **24a**] *2,3-Dimethyl-1-(methylsulfonyl)-1H-indole* **24b** (0.093 g, 0.4 mmol, 83%) as an off-white solid, mp 90–91 °C (Found: C, 58.9; H, 5.6; N, 6.2. $C_{11}H_{13}NO_2S$ requires C, 59.2; H, 5.9; N, 6.3%) [Found: M^+ (EI), 223.0684. $C_{11}H_{13}NO_2S$ requires *M*, 223.0667]; ν_{max}(KBr disc)/cm^{-1} 3048, 3011, 2927, 2854, 1457 (CH), 1352, 1174 (N–SO_2), 777 (Ar ring); δ_H(400 MHz, $CDCl_3$) 2.22 (3H, s, CH_3), 2.53 (3H, s, CH_3), 2.97 (3H, s, CH_3), 7.31 (2H, m, ArH), 7.46 (1H, m, ArH), 8.01 (1H, m, ArH); δ_C(100.6 MHz, $CDCl_3$) 9.1 (CH_3), 12.8 (CH_3), 40.4 (CH_3), 114.2 (CH), 116.2 (C), 118.7 (CH), 123.7 (CH), 124.3 (CH), 131.5 (C), 132.6 (C), 136.2 (C); *m*/*z* (EI) 223 (M^+, 55%), 208 (18), 144 (100).

3-Ethyl-1-(methylsulfonyl)-1*H*-indole 24c. [Prepared using same procedure as for **24a**] *3-Ethyl-1-(methylsulfonyl)-1H-indole* **24c** (0.049 g, 0.2 mmol, 44%) as a yellow solid, mp 63.5–65 °C (Found: C, 58.8; H, 5.8; N, 6.1. $C_{11}H_{13}NO_2S$ requires C, 59.2; H, 5.9; N, 6.3%) [Found: M^+ (EI), 223.0667. $C_{11}H_{13}NO_2S$ requires *M*, 223.0667]; ν_{max}(KBr disc)/cm^{-1} 3045, 3011, 2927, 2854, 1457 (CH), 1352, 1174 (N–SO_2), 777 (Ar ring); δ_H(400 MHz, $CDCl_3$) 1.35 (3H, t, *J* 7.6, CH_3), 2.75 (2H, dq, *J* 7.6, 1.2, CH_2), 3.05 (3H, s, CH_3), 7.21 (1H, t, *J* 1.2, ArH), 7.34 (2H, m, ArH), 7.59 (1H, d, *J* 7.6, ArH), 7.92 (1H, d, *J* 7.7, ArH); δ_C(100.6 MHz, $CDCl_3$) 13.4 (CH_3), 18.4 (CH_2), 40.4 (CH_3), 113.5 (CH), 119.9 (CH), 122.1 (CH), 123.4 (CH), 125.1 (CH), 125.4 (C), 131.3 (C), 135.7 (C); *m*/*z* (EI) 223 (M^+, 10%), 144 (100), 115 (47), 79 (53).

4-Methylsulfonyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole 24d. *N*-(2-Aminophenyl)-*N*-(2-bromocyclopent-2-en-1-yl)methanesulfonamide **23d** (497 mg, 1.5 mmol, 1 equiv.) was stirred in dichloromethane (10 ml) under nitrogen at 0 °C. Nitrosonium tetrafluoroborate (211 mg, 1.8 mmol, 1.2 equiv.) was added and the mixture was stirred for 60 min. TLC analysis showed that some starting material remained, and so additional nitrosonium tetrafluoroborate (105 mg, 1.4 mmol, 0.6 equiv.) was added. The mixture was stirred for a further 20 min, after which time no starting material remained by TLC. The solvent was removed *in vacuo,* and the resulting oil was dissolved in acetone (5 ml), and added dropwise to vigorously stirring diethyl ether (100 ml), causing immediate precipitation of the desired diazonium salt, *2-[N-(2-bromocyclopent-2-en-1-yl)-N-(methylsulfonyl)amino]benzenediazonium tetrafluoroborate* **17d** as a cream solid. During filtration the solid quickly blackened and became oily, and as a result, the salt was immediately taken on to the next stage.

2-[*N*-(2-Bromocyclopent-2-enyl)-*N*-(methylsulfonyl)amino]-benzenediazonium tetrafluoroborate **17d** from the previous step was dissolved in acetone (10 ml) and stirred under nitrogen at room temperature. Sodium iodide (225 mg, 1.5 mmol, 1 equiv.) was added and the mixture was stirred for 24 h. The solvent was removed *in vacuo* giving a brown solid, which was partitioned between dichloromethane (20 ml) and water (20 ml). The aqueous phase was extracted with dichloromethane (2 × 20 ml), and the combined organic portions were washed with water (2 × 20 ml), sodium thiosulfate (sat. aq., 20 ml) and brine (20 ml). The solution was dried over magnesium sulfate and the solvent was removed *in vacuo* to give a brown solid (394 mg). Column chromatography using ~12 g of silica and 30% diethyl ether–70% hexane, gave the desired indole, *4-methylsulfonyl-1,2,3,4-tetrahydrocyclopenta[b]indole* **24d** (230 mg, 65%) as a white solid, mp 136–137 °C (Found: C, 61.35; H, 5.54, N, 5.84. $C_{12}H_{13}NO_2S$ requires C, 61.25; H, 5.57; N, 5.95%) [Found: M^+, 235.0737. $C_{12}H_{13}NO_2S$ requires *M*, 235.0667]; ν_{max}(KBr disc)/cm^{-1} 3022, 2963, 2917, 2863, 1611; δ_H($CDCl_3$, 250 MHz) 2.48–2.57 (2H, m, CH_2), 2.74–2.81 (2H, m, CH_2), 3.01–3.08 (5H, m, CH_2, SO_2CH_3), 7.23–7.29 (2H, m, 2ArH), 7.39–7.42 (1H, m, ArH), 7.87–7.91 (1H, m, ArH); δ_C($CDCl_3$, 63 MHz) 24.2 (CH_2), 27.6 (CH_2), 27.8 (CH_2), 40.6 (CH_3), 114.1 (CH), 119.4 (CH), 123.6 (CH), 123.7 (CH), 126.6 (C), 127.4 (C), 140.5 (C), 144.0 (C); *m*/*z* (EI) 235 (M^+, 46%), 156 (100), 128 (25).

9-Methylsulfonyl-1,2,3,4-tetrahydro-9*H*-carbazole 24e (*via* the diazonium salt 17e). *N*-(2-Aminophenyl)-*N*-(2-bromocyclohex-2-enyl)methanesulfonamide **23e** (0.518 g, 1.5 mmol, 1 equiv.) was stirred in dichloromethane (10 ml) under nitrogen at 0 °C. Nitrosonium tetrafluoroborate (0.211 g, 1.8 mmol, 1.2 equiv.) was added and the mixture was stirred for 40 min. The solvent was removed *in vacuo,* and the resulting oil was dissolved in acetone (5 ml), and added dropwise to vigorously stirring diethyl ether (100 ml), causing immediate precipitation of the diazonium salt, *2-[N-(2-bromocyclohex-2-enyl)-N-methylsulfonylamino]benzenediazonium tetrafluoroborate* **17e**, as a cream solid. During filtration the solid quickly blackened and became oily, and as a result was immediately taken on to the next stage.

2-[*N*-(2-Bromocyclohex-2-en-1-yl)-*N*-methylsulfonylamino]-benzenediazonium tetrafluoroborate **17e** from the previous step was dissolved in acetone (10 ml) and stirred under nitrogen at room temperature. Sodium iodide (0.225 g, 1.5 mmol, 1 equiv.) was added and the mixture was stirred for 24 h. The solvent was removed *in vacuo* giving a brown oil, which was partitioned between diethyl ether (20 ml) and water (20 ml). The aqueous phase was extracted with diethyl ether (2 × 5 ml), and the combined organic portions were washed with water (2 × 20 ml), aq. sodium thiosulfate (20 ml) and brine (20 ml). The solution was dried over magnesium sulfate and the solvent was removed to give a brown oil. Column chromatography [8% ethyl acetate–92% hexane] gave the desired indole, *9-methylsulfonyl-1,2,3,4-tetrahydro-9H-carbazole* **24e** (185.2 mg, 54%) as an off-white solid mp 104–105 °C (Found: C, 62.53; H, 5.86, N, 5.29.

$C_{13}H_{15}NO_2S$ requires C, 62.63; H, 6.06; N, 5.62%) (Found: M^+, 249.0805. $C_{13}H_{15}NO_2S$ requires *M*, 249.0824); ν_{max}(KBr disc)/cm^{-1} 3031, 2933, 2840, 1612, 1457, 1358, 1224, 1152; δ_H($CDCl_3$, 250 MHz) 1.85–1.96 (4H, m, $2CH_2$), 2.65–2.71 (2H, m, CH_2), 2.93–2.99 (5H, m, CH_2, CH_3), 7.28–7.31 (2H, m, ArH), 7.42–7.46 (1H, m, ArH), 7.97–8.01 (1H, m, ArH); δ_C($CDCl_3$, 63 MHz) 21.2 (CH_2), 22.2 (CH_2), 23.3 (CH_2), 24.5 (CH_2), 40.3 (CH_3), 113.9 (CH), 118.3 (CH), 118.6 (C), 123.5 (CH), 124.1 (CH), 130.4 (C), 135.5 (C), 136.1 (C); *m*/*z* (EI) 249 (M^+, 63%), 170 (100%).

Isolation of 9-methylsulfonyl-1,2,3,9a-tetrahydro-9*H*-carbazole 25e from diazonium salt reaction

2-[*N*-(2-Bromocyclohex-2-enyl)-*N*-methylsulfonylamino]-benzenediazonium tetrafluoroborate **17e** (0.5 mmol) was dissolved in acetone (10 ml) and stirred under nitrogen at room temperature. Sodium iodide (75 mg, 0.5 mmol, 1 equiv.) was added and the mixture was stirred for 5 min. The solvent was removed *in vacuo* giving a brown oil, which was partitioned between ethyl acetate (20 ml) and water (20 ml). The aqueous phase was extracted with ethyl acetate (2 × 5 ml), and the combined organic portions were washed with water (2 × 20 ml), aq. sodium thiosulfate (20 ml) and brine (20 ml). The solution was dried over magnesium sulfate and the solvent was removed to give a brown oil. Column chromatography using ~9 g of silica and 20% diethyl ether–80% hexane, gave the indole, 9-methylsulfonyl-1,2,3,4-tetrahydro-9*H*-carbazole **24e**, as an off-white solid (43 mg, 35%) (data as reported above) as well as the relatively unstable alkene intermediate, *9-methylsulfonyl-1,2,3,9a-tetrahydro-9H-carbazole* **25e** (19 mg, 15%), mp 95–97 °C, δ_H($CDCl_3$, 250 MHz) 1.57–1.79 (2H, m, CH_2), 1.95–2.01 (1H, m, CH_2), 2.28–2.35 (2H, m, CH_2), 2.65–2.75 (1H, m, CH_2), 2.72 (3H, s, SO_2CH_3), 4.34–4.40 (1H, m, CHN), 5.98 (1H, m, CH=), 7.06 (1H, dd, *J* 8.1, 7.0, ArH), 7.22 (1H, dd, *J* 7.0, 7.0, ArH), 7.37 (1H, d, *J* 7.0, ArH), 7.51 (1H, d, *J* 8.1, ArH); δ_C($CDCl_3$, 100 MHz) 20.2 (CH_2), 24.7 (CH_2), 29.4 (CH_2), 34.1 (CH_3), 65.1 (CH), 114.7 (CH), 118.9 (CH), 120.5 (CH), 124.3 (CH), 129.4 (CH), 129.6 (C), 135.6 (C), 143.6 (C).

Conversion of 9-methylsulfonyl-1,2,3,9a-tetrahydro-9*H*-carbazole 25e to 9-methylsulfonyl-1,2,3,4-tetrahydro-9*H*-carbazole 24e

9-Methylsulfonyl-1,2,3,9a-tetrahydro-9*H*-carbazole **25e** (19 mg, 0.08 mmol, 1 equiv.) and toluene-4-sulfonic acid (10 mg) were stirred in benzene (2 ml) under nitrogen and the mixture heated under reflux for 2 h. TLC showed only the desired indole present, and so the solution was washed with sodium hydroxide (2 M, 5 ml) and water (5 ml) and dried over magnesium sulfate. Removal of solvent *in vacuo* gave the indole, 9-methylsulfonyl-1,2,3,4-tetrahydro-9*H*-carbazole **24e** (18 mg, 95%) as a white solid (data as reported above).

5-Methylsulfonyl-5,6,7,8,9,10,11,12-octahydrocyclonona[*b*]-indole 24f and 12-iodo-5-methylsulfonyl-5,5a,6,7,8,9,10,11,12,12a-decahydrocyclonona[*b*]indole 27

N-(2-Aminophenyl)-N-(2-bromocyclonon-2-enyl)methanesulfonamide **23f** (98 mg, 0.25 mmol, 1 equiv.) was stirred in dichloromethane (30 ml) under nitrogen at 0 °C. Nitrosonium tetrafluoroborate (35.1 mg, 0.3 mmol, 1.2 equiv.) was added and the mixture was stirred for 50 min. The solvent was removed *in vacuo*, and the resulting oil was dissolved in acetone (3 ml), and added dropwise to vigorously stirring diethyl ether (100 ml), causing immediate precipitation of *2-[N-(2-bromocyclonon-2-enyl)-N-methylsulfonylamino]benzenediazonium tetrafluoroborate* **17f** as a cream solid. During filtration the solid quickly blackened and became oily, and as a result was immediately taken on to the next stage.

2-[*N*-(2-Bromocyclonon-2-enyl)-*N*-methylsulfonylamino]-benzenediazonium tetrafluoroborate **17f** was dissolved in acetone (5 ml) and stirred under nitrogen at room temperature. Sodium iodide (37.5 mg, 0.25 mmol, 1 equiv.) was added and the mixture was stirred for 24 h. The solvent was removed *in vacuo* giving a brown oil, which was partitioned between ethyl acetate (20 ml) and water (20 ml). The aqueous phase was extracted with ethyl acetate (2 × 5 ml), and the combined organic portions were washed with water (2 × 20 ml), aq. sodium thiosulfate (20 ml) and brine (20 ml). The solution was dried over magnesium sulfate and the solvent was removed to give a brown oil. Gradient elution column chromatography using ~9 g of silica and ethyl acetate–hexane as the eluant, gave the desired indole, *5-methylsulfonyl-5,6,7,8,9,10,11,12-octahydrocyclonona[b]indole* **24f** (14.3 mg, 20%), as an off-white solid and 2 separate diastereomers of *12-iodo-5-methylsulfonyl-5,5a,6,7,8,9,10,11,12,12a-decahydrocyclonona[b]indole* **27a** and **27b** as off-white solids (13.6 mg, 13%), and (16.7 mg, 16%).

5-Methylsulfonyl-5,6,7,8,9,10,11,12-octahydrocyclonona[*b*]-indole 24f. Mp 101–102 °C (Found: C, 65.4; H, 7.0; N, 4.8. $C_{16}H_{21}NO_2S$ requires C, 65.9; H, 7.3; N, 4.8%) [Found: M^+, 291.1293. $C_{16}H_{21}NO_2S$ requires *M*, 291.1293]; ν_{max}(KBr disc)/cm^{-1} 2926, 2856, 1455, 1362, 1184; δ_H($CDCl_3$, 250 MHz) 1.11–1.33 (2H, m, CH_2), 1.40–1.57 (4H, m, CH_2), 1.64–1.89 (4H, m, CH_2), 2.79 (2H, m, CH_2), 2.93 (3H, s, SO_2CH_3), 3.11 (2H, m, CH_2), 7.26–7.30 (2H, m, ArH), 7.44–7.50 (1H, m, ArH), 8.00–8.04 (1H, m, ArH); δ_C($CDCl_3$, 63 MHz) 22.7 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 25.5 (CH_2), 26.3 (CH_2), 27.0 (CH_2), 40.1 (CH_3), 114.6 (CH), 118.6 (CH), 122.3 (C), 123.6 (CH), 124.3 (CH), 130.7 (C), 136.7 (C), 137.2 (C); *m*/*z* (EI^+) 291 (M^+, 64%), 212 (100).

12-Iodo-5-methylsulfonyl-5,5a,6,7,8,9,10,11,12,12a-decahydrocyclonona[*b*]indole 27a. Mp 138–140 °C [Found: C, 45.9; H, 5.2; N, 3.3. $C_{16}H_{22}INO_2S$ requires C, 45.8; H, 5.3; N, 3.3%] [Found: M^+, 419.0416. $C_{16}H_{22}INO_2S$ requires *M*, 419.0416]; ν_{max}(film)/cm^{-1} 2925, 2853, 1599, 1345, 1155; δ_H($CDCl_3$, 250 MHz) 1.50–1.89 (9H, m, CH_2), 2.23–2.53 (3H, m, CH_2), 3.12 (3H, s, SO_2CH_3), 3.23 (1H, dd, *J* 3.3, 3.3, CH), 4.39 (1H, ddd, *J* 10.7, 3.4, 3.4, CH), 4.62 (1H, ddd, *J* 11.3, 3.2, 3.2, CH), 7.02–7.13 (2H, m, ArH), 7.27 (1H, m, ArH), 7.38 (1H, d, *J* 8.1, ArH); δ_C($CDCl_3$, 63 MHz) 21.3 (CH_2), 23.1 (CH_2), 25.2 (CH_2), 27.8 (CH_2), 36.3 (CH_2), 36.8 (CH_2), 39.0 (CH_3), 43.8 (CH), 48.9 (CH), 65.7 (CH), 113.6 (CH), 123.7 (CH), 124.4 (CH), 129.3 (CH), 133.9 (C), 141.1 (C); *m*/*z* (CI) 437 (M + NH_4^+, 8%), 311 (52), 309 (62), 292 (61), 214 (100).

12-Iodo-5-methylsulfonyl-5,5a,6,7,8,9,10,11,12,12a-decahydrocyclonona[*b*]indole 27b. Mp 144–145 °C [Found: C, 45.9; H, 5.0; N, 3.2. $C_{16}H_{22}INO_2S$ requires C, 45.8; H, 5.3; N, 3.3%]; [Found: M + NH_4^+, 437.0760. $C_{16}H_{22}INO_2S$ requires *M* + NH_4^+, 437.0760]; ν_{max}(film)/cm^{-1} 3054, 2932, 2854, 1604; δ_H($CDCl_3$, 400 MHz) 1.41–1.89 (9H, m, CH_2), 2.04–2.09 (1H, m, CH_2), 2.26–2.31 (1H, m, CH_2), 2.38–2.42 (1H, m, CH_2), 2.89 (3H, s, SO_2CH_3), 3.76 (1H, d, *J* 11.6, C*H*Ar), 4.14 (1H, ddd, *J* 11.7, 3.2, 3.2, CHI), 4.44 (1H, dm, *J* 12.1, CHN), 7.10 (1H, dd, *J* 7.6, 7.6, ArH), 7.29 (1H, dd, *J* 8.0, 7.6, ArH), 7.41 (1H, d, *J* 8.0, ArH), 7.93 (1H, d, *J* 7.6, ArH); δ_C($CDCl_3$, 63 MHz) 18.8 (CH_2), 20.28 (CH_2), 20.34 (CH_2), 25.9 (CH_2), 32.7 (CH_2), 34.9 (CH_2), 37.1 (CH_3), 39.7 (CH), 48.1 (CH), 64.1 (CH), 115.6 (CH), 123.6 (CH), 128.5 (CH), 129.4 (CH), 132.1 (C), 141.4 (C); *m*/*z* (EI) 419 (M^+, 100%), 340 (12), 292 (64), 291 (39).

N-(2-Bromocyclohex-2-enyl)-*N*-(2-iodophenyl)methanesulfonamide 30

[Prepared using same procedure as for **22a**] *N-(2-Bromocyclohex-2-enyl)-N-(2-iodophenyl)methanesulfonamide* **30** (1.94 g, 85%) as a 14 : 1 mixture of rotamers, and as a white solid, mp

143–144 °C [Found: C, 34.37; H, 3.16, N, 2.97. $C_{13}H_{15}BrINO_2S$ requires C, 34.23; H, 3.31; N, 3.07%]; ν_{max}(KBr disc)/cm^{-1} 2946, 2933, 2906, 1650, 1577, 1340, 1166, 751; δ_H($CDCl_3$, 250 MHz) (peaks for only major rotamer mentioned in ^{1}H spectrum) 1.05–1.11 (1H, m, CH_2), 1.49–1.56 (1H, m, CH_2), 1.83–2.07 (3H, m, CH_2), 2.80–2.90 (1H, m, CH_2), 3.23 (3H, s, SO_2CH_3), 4.97–4.99 (1H, m, CHN), 6.34 (1H, t, *J* 4.3, CH=), 7.15 (1H, ddd, *J* 7.8, 7.8, 1.6, ArH), 7.36 (1H, ddd, *J* 7.8, 7.8, 1.5, ArH), 7.67 (1H, dd, *J* 7.8, 1.5, ArH), 8.01 (1H, dd, *J* 7.8, 1.4, ArH); δ_C($CDCl_3$, 63 MHz) 17.0 (CH_2), 17.9 (CH_2), 27.0 (CH_2), 27.1 (CH_2), 30.7 (CH_2), 32.2 (CH_2), 41.0 (CH_3), 42.9 (CH_3), 62.2 (CH), 63.4 (CH), 101.3 (C), 106.3 (C), 119.8 (C), 121.8 (C), 128.7 (CH), 128.9 (CH), 130.1 (CH), 132.4 (CH), 135.3 (CH), 136.1 (CH), 138.4 (CH), 139.9 (C), 141.0 (CH), 142.0 (C); *m*/*z* 475 (M + NH_4^+, 94%), 473 (M + NH_4^+, 100), 458 (M^+, 12), 456 (M^+, 10).

9-Methylsulfonyl-1,2,3,9a-tetrahydro-9*H*-carbazole 25e

To a solution of *N*-(2-bromocyclohex-2-enyl)-*N*-(2-iodophenyl)methanesulfonamide **30** (200 mg, 0.44 mmol, 1 equiv.) in dry benzene (5 ml), was added 1-ethylpiperidine hypophosphite (790 mg, 4.4 mmol, 10 equiv.) and the reaction was heated under reflux for 30 min. AIBN (28 mg, 0.17 mmol, 0.4 equiv.) was added in two portions over 30 min and the reaction was refluxed for another 20 h. The reaction was cooled before diluting with dichloromethane and extracted with water (50 ml). The organic phase was washed with aqueous hydrochloric acid, sodium bicarbonate and dried over sodium sulfate. The solvent was distilled under vacuum and the residue obtained was purified by column chromatography (5–10% ethyl acetate in hexanes) to afford a white solid identified as *9-methylsulfonyl-1,2,3,9a-tetrahydro-9H-carbazole* **25e** (65 mg, 0.26 mmol, 60%) and recovered starting material **30** (20 mg). Data as reported previously.

9-Methylsulfonyl-1,2,3,4-tetrahydro-9*H*-carbazole 24e and 9-methylsulfonyl-1,2,3,9a-9*H*-tetrahydrocarbazole 25e *via* tri-*n*-butyltin hydride reaction

N-(2-Bromocyclohex-2-enyl)-*N*-(2-iodophenyl)methanesulfonamide **30** (228 mg, 0.5 mmol, 1 equiv.) was stirred in benzene (40 ml) under nitrogen and heated under reflux. AIBN (82 mg, 0.5 mmol, 1 equiv.) and tri-*n*-butyltin hydride (0.20 ml, 0.75 mmol, 1.5 equiv.) were dissolved in benzene (10 ml) under a nitrogen atmosphere. The solution was added to the solution of **30** *via* a syringe pump over 3 h. Heating was continued for 12 h. The solvent was removed *in vacuo* to give a brown oil. Column chromatography using ~6 g of silica and ~1 l of hexane removed the bulk of the tin residues. Column chromatogaphy using 20% diethyl ether–80% hexane *gave 9-methylsulfonyl-1,2,3,4-tetrahydro-9H-carbazole* **24e** contaminated with the unrearranged alkene **25e** and some tin residues (256 mg). Further column chromatography using ~6 g of silica and 4% diethyl ether–96% hexane as the eluant gave the indole, *9-methylsulfonyl-1,2,3,4-tetrahydro-9H-carbazole* **24e** (61 mg, 49%) as a white solid and the intermediate, *9-methylsulfonyl-1,2,3,9a-tetrahydro-9H-carbazole* **25e** (32 mg, 26%), as an unstable white solid.

9-Methylsulfonyl-1,2,3,4-tetrahydro-9H-carbazole **24e**: data as described above.

9-Methylsulfonyl-1,2,3,9a-tetrahydro-9H-carbazole **25e**: data as described above.

N-(2-Bromo-1-methyl-3-phenylprop-2-enyl)-*N*-(2-iodophenyl)-methanesulfonamide 31 and *N*-(2-bromo-1-phenylbut-2-enyl)-*N*-(2-iodophenyl)methanesulfonamide 31′

To a solution of (*E*)-3-bromo-4-phenylbut-3-en-2-ol **20a** (681 mg, 3 mmol, 1 equiv.), 2-iodophenylmethanesulfonamide **16** (891 mg, 3 mmol, 1 equiv.) and triphenylphosphine (786 mg, 4.2 mmol, 1.4 equiv.) in dry tetrahydrofuran (20 ml) was added diisopropyl azodicarboxylate (0.83 ml, 4.2 mmol, 1.4 equiv.) dropwise whilst stirring under nitrogen at 0 °C. Once the addition was complete, the reaction was stirred at room temperature for 16 h. Water (20 ml) was added to quench the reaction and extracted with dichloromethane. The organic phase was washed with sodium hydroxide (2 M, 2 × 25 ml) and dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo* to yield a yellow oil. This was purified by column chromatography (silica; 20% ethyl acetate in hexanes) to afford *N-(2-bromo-1-methyl-3-phenylprop-2-enyl)-N-(2-iodophenyl)-methanesulfonamide* **31** and *N-(2-bromo-1-phenylbut-2-enyl)-N-(2-iodophenyl)methanesulfonamide* **31′** (1.1 g, 2.18 mmol, 72%) as an inseparable mixture and as a viscous yellow oil [Found: M + NH_4^+, 522.9563. $C_{17}H_{17}BrINO_2S$ requires *M* + NH_4^+, 522.9552]; ν_{max} (film)/cm^{-1} 3065, 3029, 2981, 2934, 1641, 1583, 1458, 1338, 1159; NMR showed a complex mixture of isomers: δ_H($CDCl_3$, 400 MHz) 1.38 (*J* 6.9), 1.69 (*J* 6.9), 1.76 (*J* 6.5), 1.92 (*J* 6.5) (3H, 4 × d, Me), 3.03, 3.11, 3.20, 3.35 (3H, 4 × s, CH_3), 5.12 (*J* 6.9), 5.36 (*J* 6.9), 6.47 (*J* 6.5), 6.92 (*J* 6.5) (1H, 4 × q, CHN), 5.95 and 6.13 (2 × s, =CH), 6.8–8.1 [m, 9 × ArH + =CH(partial)]; δ_C($CDCl_3$, 100.6 MHz) 16.9 (CH_3), 17.1 (CH_3), 20.0 (CH_3), 21.4 (CH_3), 42.1 (CH_3), 43.2 (CH_3), 43.3 (CH_3), 43.9 (CH_3), 62.7 (CH), 65.6 (CH), 72.8 (CH), 73.7 (CH), 103.7 (C), 106.2 (C), 107.4 (2 × C), 125.2 (CH), 126.7 (C), 127.2 (C), 127.5 (C), 127.89 (CH), 127.94 (CH), 128.10 (CH), 128.16 (CH), 128.26 (CH), 128.3 (CH), 128.6 (CH), 128.8 (CH), 128.97 (CH), 129.06 (CH), 129.1 (CH), 129.5 (CH), 129.8 (CH), 130.1 (CH), 130.3 (CH), 130.5 (CH), 130.77 (CH), 130.8 (CH), 132.5 (CH), 132.9 (CH), 133.02 (CH), 133.07 (CH), 133.2 (CH), 133.5 (CH), 134.7 (C), 135.7 (C), 135.76 (C), 140.02 (CH), 140.1 (CH), 140.28 (C), 140.3 (CH), 140.5 (CH), 141.0 (C), 141.6 (C); *m*/*z* (CI) 525 (M + NH_4^+, 100%), 523 (M + NH_4^+, 90).

3-Benzyl-2-methyl-1-(methylsulfonyl)-1*H*-indole 24a

To a solution of *N*-(2-bromo-1-methyl-3-phenylprop-2-enyl]-*N*-(2-iodophenyl)methanesulfonamide **31** and *N*-(2-bromo-1-phenylbut-2-enyl)-*N*-(2-iodophenyl)methanesulfonamide **31′** (450 mg, 0.89 mmol, 1 equiv.) in dry benzene (9 ml) was added 1-ethylpiperidine hypophosphite (1.6 g, 8.9 mmol, 10 equiv.) and the reaction was heated to reflux. AIBN (58 mg, 0.36 mmol, 0.4 equiv.) was added in two portions over 30 min and the reaction was refluxed for another 2 h. The reaction was cooled before diluting with DCM and extracted with water (50 ml). The organic phase was washed with aqueous hydrochloric acid, sodium bicarbonate and dried over anhydrous sodium sulfate. The residue was partly purified by column chromatography and the appropriate fractions obtained were dissolved in benzene (5 ml) and toluene-*p*-sulfonic acid (30 mg) was added. The reaction was heated at reflux for 1 h before diluting with dichloromethane and extracting with sodium bicarbonate solution (2 × 10 ml). The organic phase was washed with water, dried over anhydrous sodium sulfate and distilled under vacuum to yield a brown oil. This was purified by column chromatography (silica; 10% ethyl acetate in hexanes elution) to afford a single indole (**24a**) (120.5 mg, 0.40 mmol, 45.2%). Data as reported previously.

When the reaction was repeated as above but using *N*-(2-bromo-1-methyl-3-phenylprop-2-enyl-*N*-(2-iodophenyl)-methanesulfonamide (**31** + **31′**), (200 mg, 0.39 mmol, 1 equiv.), and AIBN (64 mg, 0.39 mmol, 1 equiv.), the same indole (**24a**) (50 mg, 0.16 mmol, 41%) was isolated as well as the isomeric indole, 3-ethyl-2-phenyl-1-(methylsulfonyl)-1*H*-indole **24a′** (5 mg, 0.017 mmol, 4%).

3-Ethyl-2-phenyl-1-(methylsulfonyl)-1*H*-indole 24a′. δ_H($CDCl_3$, 400 MHz) 1.19 (3H, t, *J* 7.Hz, CH_3), 2.59 (2H, q, *J* 7.6, CH_2), 2.79 (3H, s, CH_3), 7.35–7.48 (7H, m, ArH), 7.60–7.64

(1H, m, ArH), 8.12–8.15 (1H, m, ArH); δ_C($CDCl_3$, 100.6 MHz) 15.0 (CH_3), 17.9 (CH_2), 40.0 (CH_3), 115.7 (CH), 119.7 (CH), 124.2 (CH), 125.3 (CH), 125.6 (C), 128.0 (CH), 128.9 (CH), 130.7 (C), 131.1 (CH), 131.6 (C), 136.3 (C), 137.2 (C); ν_{max} ($CHCl_3$)/cm^{-1} 3065, 2969, 2935, 2878, 1606, 1496, 1458, 1376, 1175.

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17 X-Ray crystallographic data for compound **27a**, $C_{16}H_{22}INO_2S$, M 419.31. A colourless crystal was cut to 0.47 × 0.35 × 0.25 mm and mounted on a Rigaku AFC7S diffractometer at 293 K. Measurements were made using the $\omega/2\theta$ method and MoKα radiation (0.71069 Å) to a maximum 2θ of 55°. Monoclinic, space group $P2_1/n$, $a = 8.451(2)$, $b = 10.550(4)$, $c = 19.373(4)$ Å, $\beta = 93.57(2)°$, $V = 1723.9(9)$ Å^3, $Z = 4$, $\mu = 1.983$ mm^{-1}, $D_c = 1.616$ g cm^{-3}. Of 4217 measured reflections, 3956 were unique ($R_m = 4.07\%$) and 2131 observed with $I > 2\sigma(I)$. All the unique reflections were used in final refinement to convergence against F^2. $R_1 = 0.0412$, $wR_2 = 0.1186$, GOF = 0.985 for 190 parameters. Disorder in the 9-membered ring at C-11, C-12 and C-13 was modeled with isotropic atoms split over two sites. All other non-hydrogen atoms were refined anisotropically. CCDC reference number 207/439. See http://www.rsc.org/suppdata/p1/b0/b002565h/ for crystallographic files in .cif format.

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