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Radical Cyclisation onto Imidazoles and Benzimidazoles

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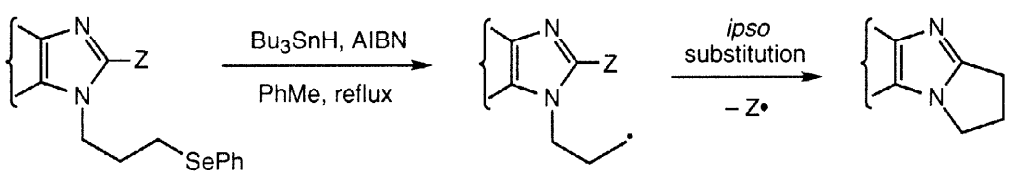
Abstract: New synthetic methodology has been developed for the synthesis of [1,2-a]fused imidazoles and benzimidazoles using intramolecular homolytic aromatic substitution. In the intramolecular substitution, *N*-(ω-alkyl) radicals are generated using Bu_3SnH from *N*-(ω-phenylselanyl)alkyl side chains. Phenylselanyl groups are used as radical leaving groups to avoid problems in the *N*-alkylation of imidazoles and benzimidazoles. Arylsulfones for imidazoles, and phenylsulfides for benzimidazoles, are used as the leaving groups in the homolytic substitutions.

The synthesis of heterocycles using radical cyclisation has become of steadily increasing importance in recent years.[1] Aromatic radical *ipso* substitution provides an attractive route to bicyclic heterocyclic compounds. Caddick *et al*[2] have recently developed a novel regioselective methodology for the synthesis of [1,2-*a*]indoles using intramolecular homolytic aromatic substitution in which SPh, SOPh or SO_2Ar groups on the indole-2-position act as radical leaving groups. Whereas bimolecular homolytic aromatic substitution is relatively unselective and therefore of limited synthetic application, *ipso* substitutions have proved useful and selective,[3] *e.g.* for substitution at the C-2 position of benzothiazoles.[4] The use of intramolecular aromatic *ipso* radical substitution with aryl-sulfones and -sulfides using tributyltin hydride (Bu_3SnH) has been gaining wider use.[2,5] In our synthetic studies of target [1,2-*a*]fused-benzimidazoles and -imidazoles with potential biological activity, we have developed a new synthetic methodology based on the protocol of Caddick *et al.*[2] Our initial studies have been published in preliminary form[6] and in this paper we describe in full the first examples of radical cyclisations onto imidazoles and benzimidazoles (Scheme 1).



Scheme 1. Synthesis of [1,2-*a*]fused imidazoles and benzimidazoles using radical *ipso*-cyclisation

Non-radical syntheses have been reported for [1,2-*a*]-fused benzimidazoles which have antitumour activity[7] and for [1,2-*a*]-fused imidazoles which have antiulcer, antidepressant and antimicrobial activity.[8] There are three general routes for the synthesis of fused bicyclic heterocycles using radical cyclisation with heteroarenes. The first route involves the cyclisation of heteroaryl radicals, generated from heteroaryl halides using Bu_3SnH, onto *N*-(ω-alkenyl) side chains, *e.g.* cyclisation of *N*-(3-butenyl)imidazol-5-yl radicals generated from the 5-bromo precursor yields the [1,2-*c*] fused imidazole.[9] Analogous cyclisations with bromo-indoles[10] and -pyridinium salts[11] have also been reported. A second route involves radical cyclisations of *N*-(ω-alkyl) radicals onto heteroarenes with oxidative re-aromatisation, *e.g.* onto the *C*-2 position of indoles,[12,13] pyrroles,[12,14] and pyridinium salts[15] and onto the *C*-5 position of imidazole-4-carbaldehydes.[14] Cyclisation onto the *C*-4 position of pyrrole with suitably attached aryl radicals proceeds by the same mechanism.[16] The third route is intramolecular *ipso*-homolytic aromatic substitution, the subject of this paper.

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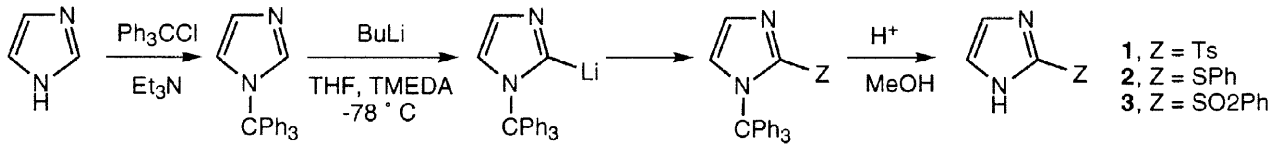
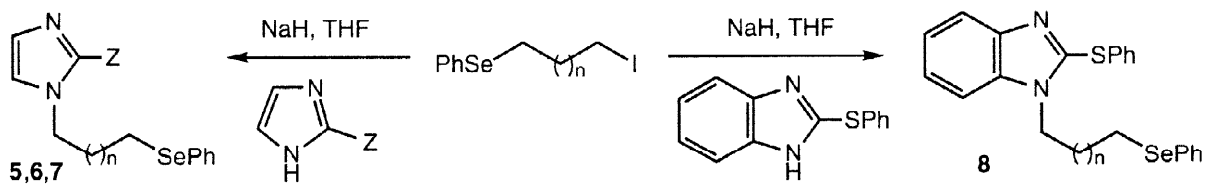
Synthesis of radical precursors

The radical leaving groups were added using standard methodology (Scheme 2). Imidazole and benzimidazole were protected using triphenylmethyl groups and treated with *n*-BuLi to form the anion at *C*-2. Treatment with tosyl fluoride[5] gave the 2-tosylimidazole (33%), whereas treatment with the cheaper tosyl chloride gave the 2-chloro analogue A better yield was obtained in the reaction with diphenyl disulfide to yield the 2-(phenylsulfanyl)imidazole (46%). The triphenylmethyl groups were removed in high yield to give **1** and **2**. 2-(Phenylsulfanyl)imidazole **2** was also converted to 2-(phenylsulfonyl)imidazole **3** using oxone™. The *C*-2 anion of 2-(triphenylmethyl)benzimidazole could only be quenched with tosyl fluoride in poor yield (11%) so 2-tosylbenzimidazole was not further used. The reaction with diphenyl disulfide (68%) followed by hydrolysis (70%) gave 2-(phenylsulfanyl)benzimidazole **4** in good yield.



Scheme 2. Synthesis of 2-tosyl- and 2-(phenylsulfanyl)-imidazole

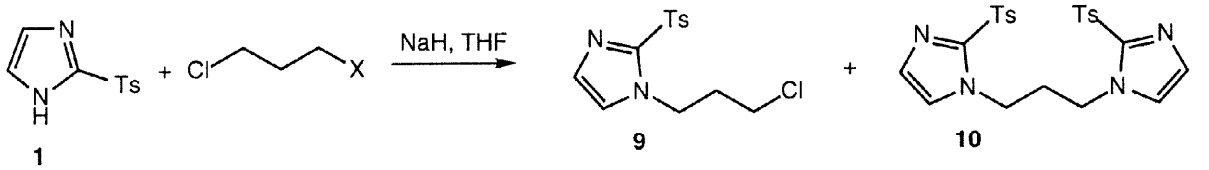
The radical precursors were prepared as shown in Scheme 3. The required ω-(phenylselanyl)alkyliodides were prepared in good yields using protocols developed in the group.[17] Monoalkylation proved facile and the required imidazole and benzimidazole radical precursors, **5** - **8**, were readily synthesised (Scheme 3).



5, Z = Ts: **a**, n = 1; **b**, n = 2; **c** n = 3; **6**, Z = SPh: n = 1; **7**, Z = $PhSO_2$, n = 1;
8, Z = SPh: **a**, n = 1; **b**, n = 2; **c**, n = 3

Scheme 3. Synthesis of radical precursors

Phenylselanides were used in place of iodine or bromine and are excellent radical leaving groups but are poor leaving groups in S_N2 reactions.[17] Caddick *et al*[2] used 1-[ω-bromo(or iodo)-alkyl]indoles as radical precursors for radical *ipso* substitution reactions. However, we found the analogous benzimidazole and imidazole precursors troublesome to prepare because of the second basic nitrogen in diazoles which caused dialkylation and other side reactions. Alkylation of 2-tosylimidazole **1** with 1,3-dibromopropene gave a single product, 1-(3-bromo-2-propenyl)-2-tosyl-1*H*-imidazole. However, alkylation of **1** with 1-bromo-3-chloropropane and 1-chloro-3-iodopropane gave alkylation on both nitrogens. When an excess of **1** was used, mixtures of the mono- and di-alkylated products **9** and **10** were obtained (Scheme 4). *N*-(3-Iodopropyl)-2-tosylimidazole, the target radical precursor, was prepared from **9** by treatment with NaI in a Finkelstein reaction, but rapidly polymerised on standing by S_N2 substitution between the imidazole-3-*N* and the pendant iodoalkane. Similar problems were encountered with alkylation reactions of 2-(phenylsulfanyl)benzimidazole.

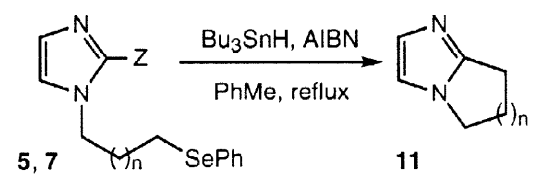


Scheme 4. X = I, **9** (53%), **10** (40%); X = Br, **9** (68%), **10** (15%)

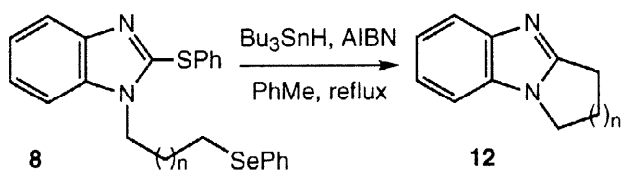
Cyclisation of *N*-[ω-(phenylselanyl)alkyl]-imidazoles and benzimidazoles

The radical precursors, *N*-[ω-(phenylselanyl)alkyl]-imidazoles and -benzimidazoles **5**, **6**, **7** and **8** were reacted under standard radical conditions with Bu_3SnH using a syringe pump (see Table 1). The 2-tosyl-imidazoles **5a-c** and the 2-(phenylsulfonyl)imidazole **7** gave reasonable yields of cyclised material with no uncyclised reduced products. Purification was aided by extraction of the basic products into acidic solution to remove the normally troublesome tributyltin residues. As expected no difference was observed for the reactions of the 2-tosylimidazole **5a** (**11a**, 52%) and the 2-(phenylsulfonyl)imidazole **7** (**11a**, 51%). However, the 2-(phenylsulfanyl)imidazole **6** only gave a poor yield of cyclised imidazole (**11a**, 16%) and a similar amount of uncyclised reduced product, 2-(phenylsulfanyl)-1-propyl-1*H*-imidazole (18%). The yields were not optimised but the reaction indicates that the phenylsulfanyl group is not sufficiently electron withdrawing to facilitate complete attack at *C*-2 by the weakly nucleophilic alkyl radical. In contrast, the 2-(phenylsulfanyl)-1*H*-benzimidazole precursors **8a-c** gave reasonable yields of cyclised [1,2-*a*]fused-benzimidazoles **12a-c**. The imidazole ring in benzimidazole is less aromatic than in imidazole and therefore addition of the intermediate radical in cyclisation is more facile and the more weakly electron withdrawing 2-(phenylsulfanyl) group is sufficient to facilitate cyclisation over reduction. The yields are comparable to the non-radical protocols reported in the literature for imidazoles[8] and benzimidazoles.[18]

Table 1. Radical cyclisation of *N*-[ω-(phenylselanyl)alkyl]-imidazoles and -benzimidazoles

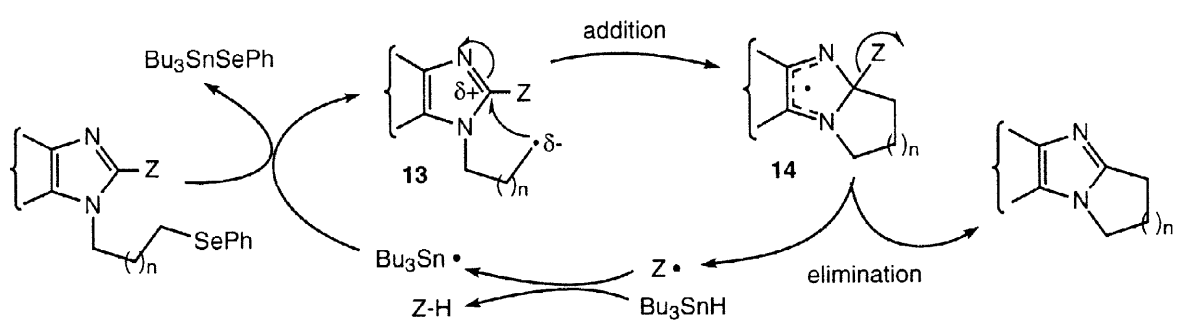


radical precursor	*product (% yield)*
5a, Z = Ts, n = 1	**11a**, 52%
5b, Z = Ts, n = 2	**11b**, 48%
5c, Z = Ts, n = 3	**11c**, 63%
7, Z = $PhSO_2$, n = 1	**11a**, 51%



8a, n = 1	**12a**, 49%
8b, n = 2	**12b**, 54%
8c, n = 3	**12c**, 17%

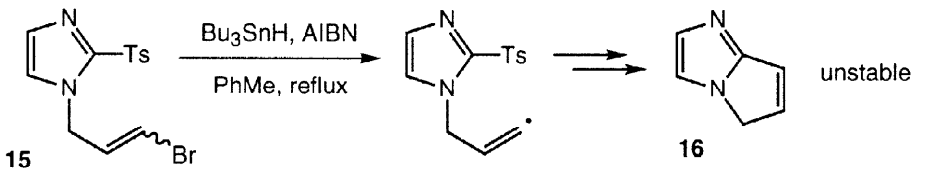
We propose the mechanism shown in Scheme 5 which is based on our results and those of Caddick *et al.*[2] The $Bu_3Sn^{\bullet}$ radicals abstract the phenylselanyl group by a S_H2 mechanism to yield the alkyl radicals **13**. The intermediate radicals **13** are weakly nucleophilic and add to the electrophilic *C*-2 carbon in the diazoles. This addition is assisted by electron withdrawing groups at *C*-2. Cyclisation onto the *C*-2 position of indoles is facilitated by phenyl-sulfonyl, -sulfinyl or -sulfanyl groups[2] and by phenylsulfanyl groups in benzimidazoles. In the more aromatic diazole, imidazole, the stronger electron withdrawing phenylsulfonyl group is required to ensure selective cyclisation over reduction. Elimination of the radical leaving group (Z• = Ts•, $PhSO_2$•, or PhS•) from intermediate **14** and aromatisation yields the cyclised products. The radical leaving group (Z•) is



Scheme 5. Putative mechanism for intramolecular aromatic homolytic substitution

strongly electrophilic and react rapidly with the nucleophilic Bu_3SnH to yield nucleophilic $Bu_3Sn^{\bullet}$ radicals which complete the radical chain reaction. This rapid interchange between sulfanyl radicals and $Bu_3Sn^{\bullet}$ radicals is well documented in the polarity studies of Roberts *et al.*[19]

Attempted cyclisation of 1-(3-bromo-2-propenyl)-2-tosyl-1*H*-imidazole **15** *via* vinyl radicals failed and an intractable mixture of products was obtained. ^{1}H NMR spectroscopy of the product mixture indicated that the expected cyclised imidazole **16** was formed, but that it decomposed rapidly and that a number of other products had been formed in the reaction (Scheme 6). Imidazole **16** has been synthesised by a non-radical route but is unstable.[20] The corresponding pyrrolo[1,2-*a*]indoles have been synthesised by radical cyclisation[2] and by non-radical routes[21] but rapidly isomerise to the 9*H*-analogues.

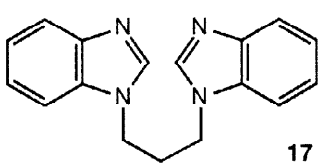


15 16

Scheme 6. Attempted cyclisation of precursor **15**

Cyclisation studies of *N*-[ω-(phenylselanyl)alkyl]benzimidazoles

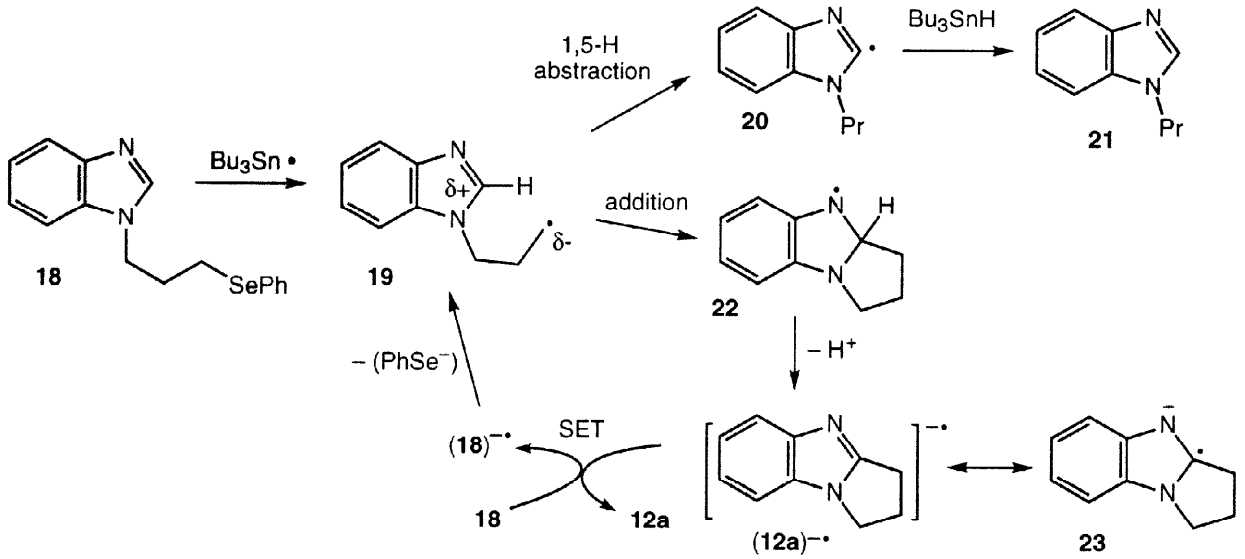
With the success of using the phenylsulfanyl groups as a leaving group in the *ipso* substitutions on benzimidazole, we also studied not using a leaving group at all on the *C*-2 position of benzimidazole in order to simplify the synthetic procedure. The alkylation of benzimidazole with 1,3-dibromopropane also gave problems of a mixture of mono- and di-alkylation and therefore a phenylselanyl precursor was used again. When an excess of benzimidazole was used, 1-{3-(1*H*-benzo[*d*]imidazol-1-yl)propyl}-1*H*-benzo[*d*]imidazole **17** was the main product and when an excess of 1,3-dibromopropane was used, 1,3-di(3-bromopropyl)-3*H*-benzo[*d*]imidazol-1-ium bromide was obtained. Both products were synthesised for characterisation. The required radical precursor, 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18** was prepared by alkylation of benzimidazole using 1-bromo-3-chloropropane and replacement of the chloro group by phenylselanide.



17

Reaction of 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18** using standard Bu_3SnH conditions gave largely the uncyclised 1-propyl-1*H*-benzimidazole **21** (89%) and a small amount of the cyclised product 2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazole **12a** (5%). The phenylsulfanyl group is required to facilitate selective addition of the intermediate alkyl radical to the *C*-2 position of benzimidazole (Table and Scheme 5). The cyclisation reaction yields **12a**, but loss of hydrogen (H•) from the cyclised intermediate **22** is unlikely, *i.e.* the mechanism shown in Scheme 5. A possible mechanism could involve reduction of the intermediate radical **22** with Bu_3SnH to yield the dihydro product which subsequently is oxidised in air during work-up to yield **12a**. This is unlikely because these dihydro benzimidazoles are stable to air oxidation over the time required for work-up and analysis.

Oxidative steps have been observed in a large number of Bu_3SnH mediated reactions[5,12-16,22,23] and a mechanism involving single electron transfer (SET) steps has been proposed.[14,22] We propose that the mechanism as shown in Scheme 7 explains the formation of **12a**. The cyclised radical **22** loses a proton to yield a stable radical anion $(\mathbf{12a})^{-\bullet}$ which undergoes SET to the starting material **18**. The radical anion $(\mathbf{12a})^{-\bullet}$ is stable because the unpaired electron resides in a π^* molecular orbital, *i.e.* delocalised over the whole aromatic system, but the canonical form **23** would be a major contributor. Proton loss would directly yield the π^* radical anion and not a radical anion with the negative charge on *C*-2 of the benzimidazole system.



Scheme 7. Oxidative radical cyclisation of 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18**

The unpaired electron in $(\mathbf{18})^{-\bullet}$ could reside in a π^* molecular orbital (MO) of either the benzimidazole ring or the phenylselanyl group. Reversible intramolecular SET between the benzimidazole π^* MO and the phenylselanyl π^* MO should be very fast. Dissociation of phenylselanyl radical anions to phenylselanide anions and alkyl radicals is well known[24] from $S_{RN}1$ reactions. Therefore, the dissociation of $(\mathbf{18})^{-\bullet}$ to phenylselanide anions and alkyl radicals **19** should also be fast. In this dissociation the unpaired electron moves from the π^* MO (as shown in **24**) to the less stable alkyl-selenium σ^* MO (as shown in **25**) prior to dissociation (Scheme 8). The π^* MO and σ^* MO are orthogonal and overlap is not allowed. The mechanism of transfer remains unknown[24] but SET between separate molecules is possible

$$\underset{\mathbf{24}}{^{-\bullet}[PhSe{-}CH_2R]}\ (Ph\ \pi^*\ MO) \underset{\text{fast}}{\overset{SET}{\rightleftharpoons}} \underset{\mathbf{25}}{[PhSe^{\bullet}{-}CH_2R]^-}\ (CH_2{-}Se\ \sigma^*\ MO) \xrightarrow[\text{fast}]{\text{dissociation}} PhSe^- + R\dot{C}H_2$$

Scheme 8. Dissociation of π^* radical anion **24**

A possible explanation for the high yield of 1-propyl-1*H*-benzimidazole could be hydrogen abstraction of the benzimidazole *H*-2 to yield the 2-benzimidazolyl radical **19**. In order to determine the amount of 1,5-hydrogen abstraction, two experiments with deuterium were carried out. Reaction between Bu_3SnH and 2-deuterio-1-[3-(phenylselanyl)-propyl]-1*H*-benzimidazole gave 2-deuterio-1-propyl-2-benzimidazole (66%, with no measurable deuterium on the side chain) and 2,3-dihydro-1*H*-benzo[*d*]pyrrolo-[1,2-*a*]-imidazole **12a** (16%). Reaction between Bu_3SnD and 1-[3-(phenylselanyl)-propyl]-1*H*-benzimidazole **17** gave 1-(3-deuterio-propyl)-benzimidazole (57%, with no measurable deuterium on the benzimidazole ring) and 2,3-dihydro-1*H*-benzo[*d*]pyrrolo-[1,2-*a*]-imidazole **12a** (17%). The results clearly show that no measurable 1,5-hydrogen abstraction is taking place. Therefore, the relative yields of the two products, **12a** and 1-propyl-1*H*-benzimidazole, is determined by the relative rate of cyclisation of intermediate radical **18** and the rate of trapping of **18** by Bu_3SnH.

In conclusion, we have developed a new facile synthetic route to polycyclic [1,2-*a*]fused azoles, which compares favourably with non radical routes. Yields were not optimised which suggests that higher yields could be obtained in syntheses using this methodology. Our results, and the results of Caddick *et al*[2] show that intramolecular aromatic homolytic *ipso* substitution provides a valuable new protocol for the synthesis of nitrogen heterocycles.

Acknowledgements

We thank Loughborough University for postgraduate studentship (F.A.), the EPSRC for a 400 MHz NMR spectrometer and the EPSRC Mass Spectrometry Unit at University of Wales, Swansea for mass spectra.

EXPERIMENTAL

General

Commercial dry solvents were used in all reactions except for light petroleum and ethyl acetate which were distilled from $CaCl_2$ and dichloromethane which was distilled over phosphorus pentoxide. Light petroleum refers to the bp 40-60 °C fraction. Sodium hydride was obtained as 60% dispersion in oil, and was washed with light petroleum, and a 2.5 M solution of *n*-butyl lithium in hexane was used in all stated cases. Melting points were determined on a Leica Galen III hot stage melting point apparatus and are uncorrected. Elemental analyses were determined on a Perkin Elmer 2400 CHN Elemental Analyser in conjunction with a Perkin Elmer AD-4 Autobalance. Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer on NaCl plates. ^1H (250 MHz) and ^{13}C (62.5 MHz) NMR spectra were recorded on a Bruker AC-250 spectrometer as solutions of $CDCl_3$ with TMS as the internal standard for ^1H NMR spectra and deuteriochloroform the standard for ^{13}C NMR spectra unless otherwise specified. Chemical shifts are given in parts per million (ppm) and *J* values in hertz (Hz). Mass spectra were recorded on a Kratos MS80 spectrometer or carried out by the EPSRC MS Service at University of Wales, Swansea. GCMS was carried out on Fisons 8000 series GCMS using a 15 m x 0.25 mm DB-5 column and an electron impact low resolution mass spectrometer. TLC using silica gel as absorbent was carried out with aluminium backed plates coated with silica gel (Merck Kieselgel 60 F_{254}), and TLC using alumina as absorbent was carried out with aluminium backed plates coated with neutral aluminium oxide (Merck 150 F_{254},TypeT). Silica gel (Merck Kieselgel 60 H silica) was used for column chromatography unless otherwise specified. Column chromatography using alumina was carried out with Aldrich aluminium oxide, activated neutral, Brockmann 1, STD Grade, 150 mesh size. Prep-TLC was carried out using aluminium oxide (Merck 60 PF_{254}, Type E).

Synthesis of radical precursors

1-(Triphenylmethyl)imidazole. Imidazole (10.2 g, 0.150 mol) was dissolved in dichloromethane (200 ml). Triphenylmethyl chloride (46.0 g, 0.165 mol) was added over 20 min and the mixture stirred until the dissolution was complete. Triethylamine (42 ml, 0.300 mol) was added slowly to the stirred solution and the stirring was continued overnight at room temperature. The solution was evaporated to dryness and the residue was recrystallised from absolute ethanol and dried to give 1-(triphenylmethyl)imidazole as colourless needles (42.0 g, 90%), mp 229-230 °C (lit.[25] mp 229-230 °C) with consistent spectroscopic data.

1-(Triphenylmethyl)benzimidazole. 1-(Triphenylmethyl)benzimidazole was prepared using the same method as for the protection of imidazole. Triphenylmethyl chloride (39 g, 0.140 mol), benzimidazole (15 g, 0.128 mol) and triethylamine (35 ml, 0.250 mol) gave a residue, which was recrystallised twice from absolute ethanol to give colourless needles of 1-(triphenylmethyl)benzimidazole (31 g, 67%), mp 181-182 °C (lit.[26] mp 180-181 °C), (Found: M^+, 360.1620. $C_{26}H_{20}N_2$ requires M, 360.1626); υ_{max}/cm^{-1} 1609, 1478, 1443, 1274, 1224, 781, 748 and 700; *m/z* 360 (M^+, 6%), 243 (100), 165 (53), 118 (24) and 91 (12).

General procedure for functionalisation at C-2.

2-Tosyl-1-(triphenylmethyl)-1H-imidazole. 1-(Triphenyl-methyl)imidazole (9.0 g, 27 mmol) was dissolved in THF (300 ml) and TMEDA (12 ml, 81 mmol) was added to the stirred solution at room temperature. The temperature of the stirred solution was lowered to -78 °C, and a solution of *n*-butyllithium (13 ml, 32 mmol) added dropwise. The solution turned red and was stirred at 0 °C for a further 20 min. A solution of *p*-toluenesulfonyl fluoride (14.1 g, 81 mmol) in THF (50 ml) was added dropwise and the stirring was continued at room temperature for a further 2 h. The solution was evaporated to dryness and saturated ammonium chloride and water added to the residue. The aqueous mixture was extracted with dichloromethane, the organic extracts dried, and the solution evaporated to dryness. The crude solid was purified by column chromatography with light petroleum and dichloromethane as eluent. Evaporation of the

eluates containing the second component gave colourless crystals of *2-tosyl-1-(triphenylmethyl)-1H-imidazole* (4.1 g, 33%), mp 175-176 °C (Found: C, 75.3; H, 5.4; N, 5.4. $C_{29}H_{24}N_2O_2S$ requires C, 75.0; H, 5.2; N, 6.0%); υ_{max} /cm^{-1} 1594, 1493, 1447, 1337, 1233, 1174 and 1148; δ_H 6.93-7.93 (3 H, m), 7.08-7.13 (4 H, m), 7.17-7.19 (6 H, m) and 7.24-7.26 (9 H, m); δ_C (62.5 MHz) 75.90 (*C*Ph$_3$), 123.64, 126.83, 127.58, 127.82, 128.19, 128.41, 129.92 and 130.10 (aromatic-CH), 133.90 (Ph-*C*), 141.93 (Ph-*C*S) and 142.23 (2-C); *m/z* 464 (M$^+$, 85%), 387 (100), 188 (40), 105 (100), 91 (27), 77 (53) and 28 (27).

2-(Phenylsulfanyl)-1-(triphenylmethyl)-1H-imidazole. 1-(Triphenylmethyl)imidazole (8.0 g, 25.8 mmol) and diphenyl disulfide (16.9 g, 77.4 mmol) gave colourless crystals of *2-(phenylsulfanyl)-1-(triphenylmethyl)-1H-imidazole* (5.0 g, 46%), mp 172-174 °C, (Found: C, 80.2; H, 5.2; N, 6.3. $C_{28}H_{22}N_2S$ requires C, 80.4; H, 5.3; N, 6.7%); υ_{max}/cm^{-1} 1580, 1492, 1479, 1446, 1415, 1233, 1112, 753, 705, 689 and 640.

2-(Phenylsulfanyl)-1-(triphenylmethyl)benzimidazole. 1-(Triphenylmethyl)benzimidazole (4.0 g, 11 mmol) and diphenyl disulfide (7.3 g, 34 mmol) were reacted for 3 h instead of 2 h to give colourless crystals of 2-(phenylsulfanyl)-1-(triphenylmethyl)benzimidazole (3.5 g, 68%), mp 182-184 °C (Found: M$^+$ 469.1734. $C_{32}H_{25}N_2S$ requires M, 469.1738); υ_{max}/cm^{-1} 1581, 1492, 1440, 1267 and 745; δ_H ; 6.00-6.02 (1 H, d, *J* 4.9, 7-H), 6.79-6.84 (1 H, ddd, *J* 0.8, 5.3, 5.3, 6-H), 6.94-6.96 (2 H, dd, *J* 1.0, 5.0), 7.05-7.09 (1 H, ddd, *J* 0.8, 5.3, 5.3, 5-H), 7.12-7.18 (3 H, m), 7.27-7.33 (9 H, m), 7.48-7.50 (6 H, m) and 7.56-7.58 (1 H, d, *J* 5.1, 4-H); δ_C (62.5 MHz) 75.90 (*C*Ph$_3$), 115.08, 119.61, 122.00, 122.31, 127.99, 123.23, 128.32, 129.18, 130.47 and 132.58 (aromatic-CH), 134.06, 137.15, 142.79, 144.24 and 153.93 (aromatic-C); *m/z* 469 (M$^+$, 31%), 243 (100), 225 (33), 165 (37) and 31 (27).

General procedure for the removal of the triphenylmethyl group.

2-tosyl-1H-imidazole **1**. 2-Tosyl-1-(triphenylmethyl)-1*H*-imidazole (3.00 g, 6.5 mmol) was dissolved in methanol and conc. hydrochloric acid (10 ml, 31-34% w/w solution) added. The solution was heated under reflux for 2 h. After cooling the solution to room temperature, most of the solvent was evaporated and the residue added to water. The acidic aqueous mixture was extracted with dichloromethane to remove the triphenylmethylalcohol. The acidic aqueous layer was evaporated to *ca.* 30-40 ml and neutralised with solid sodium carbonate. The precipitate was filtered, dried and recrystallised from absolute ethanol to yield colourless needles of *2-tosyl-1H-imidazole* **1** (0.63 g, 44%), mp 200-202 °C (lit.[27] mp 182-184 °C), (Found: C, 53.7; H, 4.1; N, 12.4. $C_{10}H_{10}N_2O_2S$ requires C, 54.0; H, 4.5; N, 12.6%); υ_{max}/cm^{-1} 1333, 1152, 1107 and 1082; δ_H ([$^2H_6$] Me_2SO) 2.36 (3 H, s, CH_3), 7.22 (2 H, brs, Im-4, 5-H), 7.40-7.43 (2 H, d, *J* 7.5 , Ar-H) and 7.77-7.80 (2 H, d, *J* 7.5 , Ar-H); δ_C ([$^2H_6$] Me_2SO) 22.96, 129.27, 132.02, 139.06, 145.34 and 46.69; *m/z* 158 (M$^+$, 100%), 131 (31), 91 (48), 77 (5), 65 (24) and 39 (12). Although the mp is different to the reported mp[27] the spectral data are in accord with literature values[27] and the combustion analysis is correct.

2-(Phenylsulfanyl)-1H-imidazole **2**. 2-(Phenylsulfanyl)-1-(triphenylmethyl)-1*H*-imidazole (4.67 g, 11.2 mmol) gave colourless needles of 2-(phenylsulfanyl)-1*H*-imidazole **2** (1.61 g, 85%), mp 175-176 °C, (Found: MH$^+$, 177.0486. $C_9H_8N_2S$ + H requires M, 177.0486); υ_{max}/cm^{-1} 2625, 1582, 1479, 1441, 1416, 1326, 1100, 964, 751 and 739; δ_H ([$^2H_6$] Me_2SO) 7.10-7.35 (7 H, m, Im-4(5)-H and Ar-H) and 12.81 (1 H, bs, NH); δ_C ([$^2H_6$] Me_2SO) 124.54, 125.40, 126.38, 128.30, 133.65 and 134.96; *m/z* 176 (M$^+$, 43%), 175 (92), 77 (88), 72 (73), 69 (35), 65 (48) and 51 (100).

2-(Phenylsulfanyl)-1H-benzimidazole **4**. 2-(Phenylsulfanyl)-1-(triphenylmethyl)benzimidazole (0.95 g, 2 mmol) gave colourless needles of 2-(phenylsulfanyl)-1*H*-benzimidazole **4** (0.32 g, 70%), mp 201-203 °C (lit.[28] mp 201.5-202.5 °C), (Found: C, 68.7; H, 4.3; N, 12.4. $C_{13}H_{10}N_2S$ requires C, 69.0; H, 4.5; N, 12.4%); υ_{max}/cm^{-1} 1618, 1477, 1442, 1413, 1349, 1266, 1235, 978, 740, 686; *m/z* 226 (60%), 225 (100), 167 (5), 155 (8), 90 (5), 77 (8) and 51 (10).

2-(Phenylsulfonyl)-1H-imidazole **3**. A solution of 2-(phenylsulfanyl)-1*H*-imidazole **2** (0.440 g, 2.5 mmol) in THF-methanol (25 ml, 1:1) was added dropwise to a solution of oxone™ (3.380 g, 5.5 mmol) at 0 °C in THF-methanol (25 ml, 1:1) and the solution was stirred at room temperature for a 48 h. The solution was filtered on a celite bed, the filtrate added to water and extracted with dichloromethane. The organic extracts were dried and evaporated to dryness to yield a solid. The residue was purified by column

chromatography with ethyl acetate as eluent to yield colourless needles of *2-(phenylsulfonyl)-1H-imidazole* **3** (0.302 g, 58%); mp 188-190 °C, (Found: M^+, 208.0307. $C_9H_8N_2O_2S$ requires M, 208.0306); υ_{max}/cm^{-1} 2764, 1446, 1330 (SO_2), 1155 (SO_2) and 1107; δ_H ([$^2H_6$]Me_2SO) 7.33 (2 H, m, Im-4(5)-H), 7.64-7.68 (2 H, m, Ar-H), 7.72-7.75 (1 H, m, Ar-H) and 7.94-7.97 (2 H, m, Ar-H); δ_C ([$^2H_6$] Me_2SO) 134.14, 136.56, 140.94, 146.84 and 149.92; *m/z* 208 (M^+, 15%), 144 (100), 117 (48), 90 (10), 77(62) and 51 (23). Further elution with ethyl acetate / methanol yielded white needles of *2-(phenylsulfinyl)-1H-imidazole* (0.101 g, 21%); mp 160-161°C, (Found: M^+, 192.0357. $C_9H_8N_2OS$ requires M, 192.0357);υ_{max}/cm^{-1} 2628, 1441, 1330, 1086 and 1054; δ_H 7.19-7.20 (2 H, m, Im-4(5)-H), 7.46-7.49 (3 H, m, Ar-H) and 7.71-7.75 (2 H, m, Ar-H); δ_C 120.20, 125.35, 129.96, 132.24, 142.79 and 146.55. *m/z* 192 (M^+, 8%), 175 (62), 144 (100), 125 (12) and 117 (39).

General procedure for the synthesis of ω-(phenylselanyl)alkyl iodides.[17]

3-Iodo-1-(phenylselanyl)propane.[17] Diphenyl diselenide (3.70 g, 11.9 mmol) was dissolved in absolute ethanol (600 ml) at room temperature. Sodium borohydride (1.00 g, 26.4 mmol) was added slowly to the stirred solution at 0 °C. After 30 min, 1-chloro-3-iodopropane (4.85 g, 23.7 mmol) added dropwise and the mixture was stirred at room temperature for 16 h. The solution was evaporated to dryness, 2 M hydrochloric acid added and the solution extracted with diethyl ether. The organic extracts were washed with sodium carbonate and brine, dried and evaporated to dryness. The residue was purified by column chromatography with light petroleum and dichloromethane as eluent to yield 3-chloro-1-(phenylselanyl)propane as a yellow oil (4.77 g, 88%); (Found: M^+, 233.9710. $C_9H_{11}ClSe$ requires M, 233.9714); υ_{max}/cm^{-1} 3072, 2956, 2940, 1579, 1478, 1304, 1233, 1072 and 739; δ_H 2.07-2.18 (2 H, m, 2'-CH_2), 3.02-3.07 (2 H, t, *J* 7.1, CH_2SePh), 3.63-3.68 (2 H, t, *J* 6.3, CH_2Cl), 7.26-7.30 (3 H, m, Ph-H) and 7.49-7.53 (2 H, m, Ph-H); δ_C 24.16 (2'-CH_2), 32.24 (PhSe*C*H_2), 43.88 (Cl*C*H_2), 126.72, 128.76, 129.13 and 132.48. 3-Chloro-1-(phenylselanyl)propane (2.50 g, 10.7 mmol) and sodium iodide (16.00 g, 0.107 mol) were added to dry acetone (250 ml) and heated under reflux for 18 h. The precipitated sodium chloride was removed by filtration on a celite bed and the solution evaporated to dryness. The residue was triturated with diethyl ether and the solution filtered a second time. The ethereal solution was evaporated to dryness to yield 3-iodo-1-(phenylselanyl)propane as a yellow-orange oil (2.69 g, 77%) which required no further purification;(Found: M^+, 325.9071. $C_9H_{11}ISe$ requires M, 325.9072); υ_{max}/cm^{-1} 3058, 2931, 1579, 1477, 1282, 1072, 1022 and 734; δ_H 2.09-2.20 (2 H, m, 2'-CH_2), 2.95-3.01 (2 H, t, *J* 7.1, CH_2SePh), 3.26-3.31 (2 H, t, *J* 6.8, CH_2I), 7.26-7.28 (3 H, m, Ph-H) and 7.49-7.51 (2H, m, Ph-H); δ_C 4.83 (CH_2I), 27.07 (2'-CH_2), 32.22 (PhSe*C*H_2), 126.08, 127.99, 128.39 and 131.96.

4-Iodo-1-(phenylselanyl)butane.[17] 1-Chloro-4-iodobutane (2.79 g, 12.8 mmol) gave 4-chloro-1-(phenylselanyl)butane[17] as a yellow oil (1.97 g, 63%); δ_H 1.82-1.94 (4 H, m, 2' and 3'-CH_2), 2.91-2.96 (2H, t, *J* 6.8, CH_2SePh), 3.51-3.56 (2 H, t, *J* 6.2, CH_2Cl), 7.24-7.30 (3 H, m, Ph-H) and 7.46-7.52 (2 H, m, Ph-H); δ_C (62.5 MHz) 26.91, 27.19, 32.34 (PhSe*C*H_2), 44.27 (Cl*C*H_2), 126.86, 127.66, 129.02, 129.13, 131.46 and 132.65. 4-Chloro-1-(phenylselanyl)butane (1.80 g, 7.3 mmol) gave 4-iodo-1-(phenylselanyl)butane as a yellow-orange oil (1.92 g, 78%); (Found: M^+, 339.9227. $C_{10}H_{13}ISe$ requires M, 339.9227). The oil rapidly darkens on standing at room temperature and was used shortly after synthesis. IR, ^1H and ^{13}C NMR and MS were consistent with literature values for both compounds.

5-Iodo-1-(phenylselanyl)pentane. 1-Chloro-5-iodopentane (2.98 g, 12.6 mmol) gave 5-chloro-1-(phenylselanyl)pentane as a yellow oil (2.94 g, 89%) which required no further purification; υ_{max}/cm^{-1} 1579, 1477, 1436, 1300, 1073, 1022, 735 and 691; δ_H 1.61-1.64 (2 H, m, 3'-CH_2), 1.75-1.83 (4 H, m, 2' and 4'-CH_2), 2.94-2.97 (2 H, t, *J* 7.3, CH_2SePh), 3.53-3.56 (2 H, t, *J* 6.5, CH_2Cl), 7.27-7.32 (3 H, m, Ph-H) and 7.52-7.55 (2 H, m, Ph-H); δ_C 27.26 (3'-CH_2), 27.68, 28.29, 32.54 (PhSe*C*H_2), 45.17 (Cl*C*H_2), 127.11, 129.17, 129.43, 130.74 and 133.01. 5-Chloro-1-(phenylselanyl)pentane (1.80 g, 6.9 mmol) gave *5-iodo-1-(phenylselanyl)pentane* as a yellow-orange oil (1.56 g, 64%); (Found: M^+, 353.9384. $C_{11}H_{15}ISe$ requires M, 353.9385);υ_{max}/cm^{-1} 2253, 1478, 1438, 1199, 1023, 909, 733, 692 and 650; δ_H 1.49-1.58 (2 H, m, 3'-CH_2), 1.67-1.86 (4 H, m, 2' and 4'-CH_2), 2.88-2.94 (2 H, t, *J* 7.3, CH_2SePh), 3.14-3.19 (2 H, t, *J* 7.0, CH_2I), 7.25-7.31 (3 H, m, Ph-H) and 7.48-7.52 (2 H, m, Ph-H); δ_C 7.42 (CH_2I), 28.55, 30.09, 31.65, 33.95 (PhSe*C*H_2), 127.76 , 130.05, 132.52, 133.55 and 133.59; *m/z* 354 (M^+, 6%), 227 (37), 171 (18), 157 (87), 91 (48), 77 (76), 69 (97) and 41 (100).

General method for alkylation of imidazoles and benzimidazoles.

1-[3-(Phenylselanyl)propyl]-2-Tosyl-1H-imidazole **5a**. 2-Tosyl-1*H*-imidazole **1** (0.121 g, 0.55 mmol) was added to a suspension of sodium hydride (16 mg, 0.66 mmol) in acetonitrile (150 ml). The mixture was stirred and heated under reflux for 1 h and 3-iodo-1-(phenylselanyl)propane (0.180 g, 0.55 mmol) was added. The mixture was stirred and heated under reflux for a further 2 h. The salts formed were removed by filtration on a celite bed and the solution was evaporated to dryness. The resulting crude product was purified by column chromatography with diethyl ether and light petroleum as eluent to yield yellow crystals of *1-[3-(phenylselanyl)propyl]-2-tosyl-1H-imidazole* **5a** as a yellow oil (0.110 g, 48%); (Found: M$^+$, 420.0413. $C_{19}H_{20}N_2O_2SSe$ requires M, 420.0410); υ_{max}/cm^{-1} 1596, 1579, 1478, 1438, 1332, 1293, 1266, 1148 (SO_2), 736 and 658; δ_H 2.13-2.24 (2 H, m, 2'-CH_2), 2.40 (3 H, s, CH_3), 2.82-2.88 (2 H, t, *J* 7.1, CH_2SePh), 4.41-4.47 (2 H, t, *J* 7.1, NCH_2), 6.94 (1 H, s, Im-4(5)-H), 7.08 (1 H, s, Im-4(5)-H), 7.25-7.28 (3 H, m, SePh-H), 7.30-7.33 (2 H, d, *J* 7.5 , Ar-H), 7.46-7.50 (2 H, m, SePh-H) and 7.87-7.90 (2 H, d, *J* 7.5, Ar-H); δ_C (62.5 MHz) 21.63 (CH_3), 23.84 (2'-CH_2), 31.35 (PhSe*C*H_2), 47.49 (N*C*H_2), 124.15, 127.25, 128.19, 129.21, 129.66, 129.87, 132.87, 136.67, 143.33 and 146.00; *m/z* 265 (100%), 155 (13), 108 (17), 91 (72), 41 (21) and 65 (66).

1-[4-(Phenylselanyl)butyl]-2-tosyl-1H-imidazole **5b**. 2-Tosyl-1*H*-imidazole **1** (0.195 g, 0.88 mmol) and 4-iodo-1-(phenylselanyl)butane (0.289 g, 0.88 mmol) gave *1-[4-(phenylselanyl)-butyl]-2-tosyl-1H-imidazole* **5b** as cream coloured crystals (0.156 g, 41%), mp 105-107 °C (Found: M$^+$, 434.0567. $C_{20}H_{22}N_2O_2SSe$ requires M, 434.0567); υ_{max}/cm^{-1} 2915, 1598, 1478, 1463, 1430, 1330 (SO_2), 1296, 1148 and 788; δ_H 1.67-1.74 (2 H, m, 3'-CH_2), 1.91-1.98 (2 H, m, 2'-CH_2), 2.43 (3 H, s, CH_3), 2.86-2.92 (2 H, t, *J* 7.1, CH_2SePh), 4.30-4.36 (2 H, t, *J* 7.3, NCH_2), 6.95 (1 H, s, Im-4(5)-H), 7.11 (1 H, s, Im-4(5)-H), 7.25-7.28 (3 H, m, SePh-H), 7.33-7.36 (2 H, d, *J* 7.5, Ar-H), 7.46-7.50 (2 H, m, SePh-*o*-H) and 7.89-7.92 (2 H, d, *J* 7.5 , Ar-H); δ_C (62.5 MHz) 21.63 (CH_3), 26.81 (3'-CH_2), 26.95 (2'-CH_2), 31.09 (PhSe*C*H_2), 47.44 (N*C*H_2), 123.93, 126.98, 127.97, 128.13, 129.62, 129.87, 132.76, 132.79, 136.80, 143.60 and 145.14; *m/z* 434 (M$^+$, 4%), 279 (30), 223 (12), 157 (20), 122 (21) and 91 (100).

1-[5-(phenylselanyl)pentyl]-2-tosyl-1H-imidazole **5c**. 2-Tosyl-1*H*-imidazole **1** (0.130 g, 0.59 mmol), and 5-iodo-1-(phenylselanyl)pentane (0.208 g, 0.59 mmol) gave *1-[5-(phenylselanyl)pentyl]-tosyl-1H-imidazole* as **5c** colourless crystals (0.132 g, 50%), mp 83-85 °C (Found: M$^+$, 448.0724. $C_{21}H_{24}N_2O_2SSe$ requires M, 448.0723); υ_{max}/cm^{-1} 2937, 1578, 1477, 1460, 1432, 1326 (SO_2), 1174 (SO_2), 1074, 813 and 796; δ_H 1.32-1.45 (2 H, m, 3'-CH_2), 1.68-1.81 (4 H, m, 2' and 4'-CH_2), 2.38 (3 H, s, CH_3), 2.85-2.88 (2 H, t, *J* 7.3, CH_2SePh), 4.27-4.31 (2 H, t, *J* 7.4, NCH_2), 6.95 (1 H, s, Im-4(5)-H), 7.10 (1 H, s, Im-4(5)-H), 7.22-7.27 (3 H, m, SePh-H), 7.30-7.32 (2 H, d, *J* 7.5 , Ar-H), 7.46-7.48 (2 H, m, SePh-H) and 7.88-7.90 (2 H, d, *J* 7.5, Ar-H); δ_C 21.93 (CH_3), 26.93 (3'-CH_2), 27.67 (4'-CH_2), 30.21, 31.15, 48.37 (N*C*H_2), 124.50, 127.23, 128.44, 129.24, 130.30, 130.64, 132.81, 137.44, 143.49, 145.52 and 153.18; *m/z* 448 (M$^+$, 16%), 293 (29), 223 (49), 157 (30), 136 (28) and 91(100).

1-[3-(Phenylselanyl)propyl]-2-(phenylsulfanyl)-1H-imidazole **6**. 2-(Phenylsulfanyl)-1*H*-imidazole **2** (0.470 g, 2.67 mmol) and 3-iodo-1-(phenylselanyl)propane (0.870 g, 2.67 mmol) gave **6** as a yellow oil (0.555 g, 56%); υ_{max}/cm^{-1} 2940, 1580, 1478, 1458, 1438, 1428, 1027, 1023 and 690; δ_H 1.95-2.06 (2 H, m, 2'-CH_2), 2.71-2.76 (2 H, t, *J* 7.0, CH_2SePh), 4.09-4.14 (2 H, t, *J* 7.0, NCH_2), 7.04 (2 H, m, Im-4(5)-H), 7.14-7.29 (8 H, m, Ar-H) and 7.42-7.46 (2 H, m, Ar-H); δ_C 23.98 (2'-CH_2), 30.80 (PhSe*C*H_2), 46.36 (N*C*H_2), 122.43, 126.61, 127.22, 128.03, 129.16, 130.52 and 132.97.

1-[3-(Phenylselanyl)propyl]-2-(phenylsulfonyl)-1H-imidazole **7**. The imidazole **3** (0.136 g, 0.65 mmol) and 1-(phenylselanyl)-3-iodopropane (0.212 g, 0.65 mmol) gave **7** as a yellow oil (0.214 g, 81%), (Found: M$^+$, 406.0254. $C_{18}H_{18}N_2O_2SSe$ requires M, 406.0254); δ_H 2.10-2.21 (2 H, m, 2'-CH_2), 2.80-2.86 (2 H, t, *J* 7.1, CH_2SePh), 4.40-4.46 (2 H, t, *J* 7.1, NCH_2), 6.95 (1 H, m, Im-4(5)-H), 7.09 (1 H, m, Im-4(5)-H), 7.25-7.27 (3 H, m, SePh-H), 7.45-7.49 (2 H, m, SePh-H), 7.50-7.53 (2 H, d, *J* 7.5, Ar-H), 7.57-7.63 (1 H, m, Ar-H), 7.97-8.00 (2 H, d, *J* 7.5, Ar-H); δ_C (62.5 MHz) 23.92 (2'-CH_2), 31.50 (PhSe*C*H_2), 47.68 (N*C*H_2), 124.55, 127.38, 128.14, 129.22, 129.35, 130.00, 132.99, 134.10, 139.93, 142.79; *m/z* 406 (M$^+$, 100%), 376 (30), 329 (14), 305 (41), 284 (45), 265 (100), 157 (23) and 77 (66).

1-[3-(Phenylselanyl)propyl]-2-(phenylsulfanyl)-1H-benzimidazole **8a**. The benzimidazole **4** (0.650 g, 3.0 mmol) and 1-(phenylselanyl)-3-iodopropane (0.730 g, 2.3 mmol) gave **8a** as a yellow oil (0.560 g, 44%) (Found: M^+, 424.0525. $C_{22}H_{20}N_2SSe$ requires M, 424.0525); υ_{max}/cm^{-1} 1579, 1478, 1423, 1355, 1248, 1023, 909, 739 and 690; δ_H 2.04-2.15 (2 H, m, 2'-CH_2), 2.81-2.86 (2 H, t, *J* 6.9, CH_2SePh), 4.31-4.37 (2 H, t, *J* 7.1, NCH_2), 7.24-7.33 (8 H, m, Ar-H), 7.41-7.49 (4 H, m, Ar-H), 7.77-7.81 (2 H, m, Ar-H); δ_C 23.48 (2'-CH_2), 28.79 (PhSe*C*H_2), 43.27 (N*C*H_2), 108.68, 119.07, 121.49, 122.33, 126.31, 129.94, 128.36, 129.66, 131.07, 132.04, 134.86, 144.48 and 146.61; *m/z* 424 (M^+, 34%), 315 (43), 267 (88), 239 (50), 157 (26), 129 (33), 109 (48), 77 (100) and 51 (75).

1-[4-(Phenylselanyl)butyl]-2-(phenylsulfanyl)-1H-benzimidazole **8b**. The benzimidazole **4** (0.265 g, 1.17 mmol), sodium hydride (42 mg, 1.76 mmol) and 1-(phenylselanyl)-4-iodobutane (0.300 g, 0.88 mmol) gave **8b** as a yellow oil (0.228 g, 44%); (Found: M^+, 438.0669. $C_{23}H_{22}N_2SSe$ requires M, 438.0668); υ_{max}/cm^{-1} 1581, 1479, 1462, 1438, 1424, 1360, 1279, 1024, 907 and 733; δ_H 1.24-1.57 (2 H, m, 3'-CH_2), 1.60-1.75 (2 H, m, 2'- CH_2), 2.68-2.74 (2 H, t, *J* 7.1, CH_2SePh), 4.06-4.11 (2 H, t, *J* 7.2, NCH_2), 7.11-7.21 (8 H, m, Ar-H), 7.27-7.33 (4 H, m, Ar-H), 7.65-7.69 (2 H, m, Ar-H); δ_C (62.5 MHz) 27.08 (3'-CH_2), 27.16 (2'-CH_2), 30.35 (PhSe*C*H_2), 44.11 (N*C*H_2), 109.66, 119.94, 122.33, 123.19, 127.01, 129.39, 129.67, 130.43, 132.91, 135.67, 143.40; *m/z* 438 (M^+, 54%), 281 (100), 239 (46), 225 (70), 171 (50), 157 (43), 109 (48), 91 (58), 77 (94) and 51 (47).

1-[5-(Phenylselanyl)pentyl]-2-(phenylsulfanyl)-1H-benzimidazole **8c**. The benzimidazole **4** (0.661 g, 2.92 mmol), sodium hydride (0.105 g, 4.39 mmol) and 1-(phenylselanyl)-5-iodopentane (1.034 g, 2.92 mmol) gave **8c** as a yellow oil (0.992 g, 75%); (Found: M^+, 452.0825. $C_{24}H_{24}N_2SSe$ requires M, 452.0825); υ_{max}/cm^{-1} 1579, 1478, 1422, 1355, 1266, 1023, 738, 690; δ_H 1.41-1.44 (2 H, m, 3'-CH_2), 1.65-1.71 (4 H, m, 2' and 4'-CH_2), 2.80-2.86 (2 H, t, *J* 7.3, CH_2SePh), 4.18-4.24 (2 H, t, *J* 7.4, NCH_2), 7.25-7.31 (8 H, m, Ar-H), 7.39-7.49 (4 H, m, Ar-H), 7.77-7.79 (2 H, m, Ar-H); δ_C (62.5 MHz) 26.84 (3'-CH_2), 27.34 (4'-CH_2), 29.00 (2'-CH_2), 29.64 (PhSe*C*H_2), 44.53 (N*C*H_2), 109.70, 119.85, 122.29, 123.19, 126.79, 129.03, 130.52, 132.52, 135.70, 143.25, 147.43; *m/z* 452 (M^+, 6%), 295 (16), 225 (28), 206 (12), 158 (35), 157 (35) and 91 (43).

1-(3-Bromo-2-propenyl)-2-tosyl-1H-imidazole. 2-Tosyl-1*H*-imidazole **1** (0.600 g, 2.7 mmol) and 1,2-dibromopropene (mixture of *cis* and *trans* isomers, 1.620 g, 8.1 mmol) gave yellow crystals of *1-(3-bromo-2-propenyl)-2-tosyl-1H-imidazole* (0.920 g, 77%), as a mixture of *cis* and *trans* isomers in a ratio similar to that of the starting dibromopropene, mp 99-100 °C [Found: $(M+H)^+$, 340.9825. $C_{13}H_{13}N_2BrO_2S$ requires M, 340.9825]; υ_{max}/cm^{-1} 1624, 1594, 1329 (SO_2), 1152, 1147 (SO_2) and 782; δ_H 2.40 (3 H, s, CH_3), 4.92-4.94 (2 H, d, *J* 5.0, 1'-*cis* CH_2), 5.09-5.12 (2 H, dd, *J* 1.5 Hz and *J* 6.5, 1'-*trans*-CH_2), 6.24-6.33 (1 H, m, 2'-*cis* and *trans*-H), 6.43-6.47 (1 H, m, 3'-*cis* and *trans*-H), 7.04 (1 H, d, *J* 0.8, Im-4(5)-H), 7.10 (1 H, d, *J* 0.8, Im-4(5)H), 7.31-7.35 (2H, d, *J* 7.5, Ar-H) and 7.87-7.90 (2 H, d, *J* 7.5 , Ar-H); δ_C 22.08 (CH_3), 47.30 (1'-*cis* - CH_2), 49.56 (1'-*trans*-CH_2), 111.57, 112.96, 124.18-124.37 (Im-CH), 128.71, 129.48 (2'-*cis* and *trans*-H), 130.37 and 130.47; *m/z* 341 (M^+, 5%), 277 (77), 197 (100), 155 (5), 119 (12), 106 (46), 65 (20) and 39 (33).

1-(3-Iodopropyl)-2-tosyl-1H-imidazole. 2-Tosyl-1*H*-imidazole **1** (0.260 g, 1.17 mmol) and 1-bromo-3-chloropropane (0.35 ml, 3.51 mmol) gave 1-[3-chloropropyl]-2-tosyl-1*H*-imidazole **9** as a yellow needles (0.348 g, 68%) mp 68-69 °C (Found: M^+, 298.0543. $C_{13}H_{15}N_2ClO_2S$ requires M, 298.0543); υ_{max}/cm^{-1} 3137, 2922, 1328 (SO_2), 1145 (SO_2), 658 and 600; δ_H 2.32-2.39 (2 H, m, 2'-CH_2), 2.44 (3 H, s, CH_3), 3.51-3.58 (2 H, t, *J* 6.3, CH_2Cl), 4.51-4.56 (2 H, t, *J* 6.3, NCH_2), 7.07 (1 H, s, Im-4(5)-H), 7.12 (1 H, s, Im-4(5)-H), 7.34-7.37 (2 H, d, *J* 7.5, Ar-H) and 7.90-7.93 (2 H, d, *J* 7.5 , Ar-H); δ_C 20.15 (CH_3), 32.07 (2'-CH_2), 39.75 (*C*H_2Cl), 43.72 (N*C*H_2), 123.08, 126.81, 128.18, 128.23, 135.25, 141.79 and 143.81 (q-C); *m/z* 299 (MH^+, 3%), 249 (3), 199 (34), 172 (100), 152 (15), 91 (94), 77 (13), 65 (48) and 41 (39); and 1,3-di-(2-tosyl-imidazolyl)propane **10** as colourless needles (87 mg, 15%); δ_H 2.44 (6 H, s, CH_3), 2.47-2.50 (2 H, m, 2'-CH_2), 4.41-4.47 (4 H, t, *J* 7.5, NCH_2), 7.04 (2 H, s, Im-4(5)-H), 7.14 (2 H, s, Im-4(5)-H), 7.35-7.38 (4 H, d, *J* 7.5, ArH) and 7.88-7.91 (4 H, d, *J* 7.5, ArH). When 1-chloro-3-iodopropane was used in place of 1-bromo-3-chloropropane yields of 1-[3-chloropropyl]-2-tosyl-1*H*-imidazole **9** (53%) and 1,3-di-(2-tosylimidazolyl)-propane **10** (40%) were obtained.

1-[3-Chloropropyl]-2-tosyl-1*H*-imidazole **9** (0.110 g, 0.36 mmol) and sodium iodide (0.270 g, 1.80 mmol) were added to dry acetonitrile (50 ml) and heated under reflux for 6 h. The precipitated sodium chloride was removed by filtration on a celite bed, and the solution was evaporated to dryness. The residue was added to saturated sodium sulfite solution and extracted with dichloromethane. The organic extracts were dried and evaporated to dryness. The residue was purified by column chromatography with ethyl acetate and light petroleum as eluent to yield colourless needles of 1-(3-iodopropyl)-2-tosyl-1*H*-imidazole (42 mg, 30%), (Found: MH^+ 390.9977. $C_{13}H_{15}N_2IO_2S$+H requires M, 389.9979); υ_{max}/cm^{-1} 3111, 2925, 1596, 1330 (SO_2), 1293, 1186, 1147 and 1082; δ_H 2.34-2.42 (2 H, m, 2'-CH_2), 2.45 (3 H, s, CH_3), 3.12-3.17 (2 H, t, *J* 6.3, CH_2I), 4.45-4.51 (2 H, t, *J* 7.5, NCH_2), 7.09 (1 H, s, Im-4(5)-H), 7.12 (1 H, s, Im-4(5)-H), 7.36-7.39 (2 H, d, *J* 7.5, Ar-H) and 7.91-7.94 (2 H, d, *J* 7.5, Ar-H); δ_C 0.00 (CH_2I), 20.03 (CH_3), 32.62 (2'-CH_2), 46.67 (NCH_2), 122.66, 126.69, 128.06, 128.27, 141.63 and 143.69; *m/z* 391 (MH_2^+, 38%), 265 (8), 223 (9), 111 (16), 109 (100) and 69 (8). The iodide rapidly darkened to unidentifiable products on standing at room temperature.

Cyclisation of *N*-[ω-(phenylselanyl)alkyl]-imidazoles and -benzimidazoles

Standard procedure for radical cyclisation reactions.

6,7-Dihydro-5H-pyrrolo[1,2-a]imidazole **11a**. All reactions were deoxygenated by passing a stream of nitrogen through the solutions for 30 min. Reactions were carried out under an atmosphere of nitrogen. A solution of Bu_3SnH (0.1 ml, 0.35 mmol) and AIBN (30 mg, 0.18 mmol) in toluene (30 ml) was added to 1-[3-(phenylselanyl)propyl]-2-tosyl-1*H*-imidazole **5a** (95 mg, 0.23 mmol) in toluene (100 ml) at reflux over 5 h. The solution was stirred and heated under reflux for a further 1 h. After cooling to room temperature, the solution was evaporated to dryness and hydrochloric acid (2 M, 50 ml) was immediately added. The aqueous solution was washed thoroughly with light petroleum and basified to pH 8 with saturated sodium carbonate solution followed by basification with aqueous sodium hydroxide solution (2 M) to pH 14. The aqueous solution was extracted into dichloromethane and the organic extracts dried and evaporated to dryness to yield a brown oil residue which was placed under an atmosphere of nitrogen. The residue was analysed using TLC and ^1H NMR spectroscopy which showed a complete conversion of the starting bromide. Further purification of the colourless crystals of 6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole **11a** was not required (13 mg, 52 %), mp 72-73 °C (lit.[8] 72.5-75.5 °C); δ_H 2.57-2.68 (2 H, m, 6-CH_2), 2.83-2.89 (2 H, t, *J* 7.5, 7-CH_2), 3.94-3.99 (2 H, t, *J* 7.0, NCH_2), 6.87 (1 H, s, Im-2-H) and 7.04 (1 H, s, Im-3-H); δ_C 23.41 (6-CH_2), 26.77 (7-CH_2), 45.00 (NCH_2), 114.88 (C-2), 133.41 (C-3) and 155.10 (C-7a).

Using the standard procedure for radical cyclisation, 1-[3-(phenylselanyl)propyl]-2-(phenylsulfonyl)-imidazole **7** gave **5a** (51%) as a colourless oil which required no further purification.

5,6,7,8-Tetrahydroimidazo[1,2-a]pyridine **11b**. 1-[3-(Phenylselanyl)butane]-2-tosyl-1*H*-imidazole **5b** (0.427 g, 0.98 mmol) was reacted using the standard conditions for radical cyclisation for 10 h to yield 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine[8] (57 mg, 48%) as a colourless oil which required no further purification; δ_H 1.89-1.97 (4 H, m, 6 and 7-CH_2), 2.82-2.87 (2 H, t, *J* 6.0, 8-CH_2), 3.90-3.95 (2 H, t, *J* 5.6, NCH_2), 6.75 (1 H, s, Im-3-H) and 6.94 (1 H, s, Im-2-H); δ_C 21.21 (C-7), 23.54 (6-CH_2), 24.95 (8-CH_2), 45.09 (NCH_2), 118.27 (C-2), 135.57 (C-3) and 145.21 (C-8a).

6,7,8,9-Tetrahydro-5H-imidazo[1,2-a]azepine **11c**. 1-[5-(Phenylselanyl)pentyl]-2-tosyl-1*H*-imidazole **5c** (0.125 g, 0.28 mmol) was reacted using the standard conditions for radical cyclisation for 10 h to yield 6,7,8,9-tetrahydro-5*H*-imidazo[1,2-*a*]azepine[8] **11c** (32 mg, 63%) as a colourless oil which required no further purification; δ_H 1.64-1.80 (6 H, m, 6, 7, 8-CH_2), 2.87-2.92 (2 H, m, 9-CH_2), 3.90-3.94 (2 H, m, NCH_2), 6.74 (1H, s, Im-2(3)-H) and 6.79 (1 H, s, Im-2(3)-H); δ_C 22.56 (C-7), 26.11 (C-8), 29.40 (C-6), 30.11 (C-9), 48.77 (NCH_2), 119.22 (C-2), 126.21 (C-3) and 150.90 (C-9a).

Radical cyclisation of 1-[3-(phenylselanyl)propyl]-2-(phenylsulfanyl)-1H-imidazole **6**. 1-[3-(Phenylselanyl)propyl]-2-(phenylsulfanyl)-1*H*-imidazole **7** (0.547 g, 1.46 mmol) yielded a mixture of 6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole **11a** (16%) and 2-(phenylsulfanyl)-1-propyl-1*H*-imidazole (18%); δ_H 0.80-0.86 (3 H, t, *J* 7.4, CH_3), 1.62-1.70 (2 H, m, 2'-CH_2), 3.92-3.96 (2 H, t, *J* 6.8, NCH_2) and 7.02-7.56 (7 H, m, Im-H

and Ph-H); The yields were measured using ^{1}H NMR spectral analysis with 1,4-dimethoxybenzene as internal standard.

2,3-Dihydro-1H-benzo[d]pyrrolo[1,2-a]imidazole **12a**. 1-[3-(Phenylselanyl)propyl]-2-(phenylsulfanyl)-1*H*-benzimidazole **8a** (0.450 g, 1.06 mmol) gave **12a** as colourless crystals (83 mg, 49%), mp 105-107 °C (lit.[18], mp 114-115 °C) (Found: M$^+$, 158.0844. $C_{10}H_{10}N_2$ requires M, 158.0844); δ_H 2.66-2.78 (2 H, m, C-3), 3.04-3.10 (2 H, t, *J* 7.5, C-2), 4.08-4.14 (2 H, t, *J* 7.0, NCH_2), 7.17-7.33 (3 H, m, Ar-H), 7.68-7.72 (1 H, m, Ar-H); δ_C 23.89 (3'-CH_2), 26.48 (2'-CH_2), 43.12 (NCH_2), 109.86, 119.99, 122.05, 122.14, 132.79, 149.30 and 161.55; *m/z* 158 (M$^+$, 96%), 157 (100), 130 (16), 129 (14), 103 (24), 102 (15), 86 (25), 84 (38) and 51 (31).

1,2,3,4-Tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine **12b**. 1-[4-(Phenylselanyl)butyl]-2-(phenylsulfanyl)-1*H*-benzimidazole **8b** (0.184 g, 0.42 mmol) yielded colourless crystals of **12b** (39 mg, 54%), mp 98-100 °C (lit.[18] mp, 99.8-100.1°C) which required no further purification; (Found: M$^+$, 172.1000. $C_{11}H_{12}N_2$ requires M, 172.1000); IR, ^{1}H NMR, ^{13}C NMR and MS spectral data were consistent.

7,8,9,10-Tetrahydro-6H-benzo[4,5]imidazo[1,2-a]azepine **12c**. 1-[5-(Phenylselanyl)pentyl]-2-(phenylsulfanyl)-1*H*-benzimidazole **8c** (0.465 g, 1.03 mmol) was reacted using the standard conditions for 10 h to yield colourless crystals of **12c** (31 mg, 17%), mp 124-125 °C (lit.[18] mp, 124-125 °C); δ_H 1.73-1.95 (6 H, m), 3.07-3.11 (2 H, m), 4.14-4.18 (2 H, m, NCH_2), 7.18-7.28 (3 H, m, Ar-H), 7.65-7.69 (1 H, m, Ar-H); δ_C 27.53, 30.71, 31.85, 32.87, 46.51, 110.66, 121.17, 124.08, 124.47, 137.76, 144.21 and 150.29.

Attempted cyclisation of 1-(3-bromo-2-propenyl)-2-tosyl-1H-imidazole **15**. 1-(3-Bromo-2-propenyl)-2-tosyl-1*H*-imidazole was reacted using the standard conditions to yield and intractable brown oil residue. TLC and ^{1}H NMR spectroscopic analysis showed full conversion of the starting material to unidentifiable products.

Cyclisation studies of *N*-[ω-(phenylselanyl)alkyl]benzimidazoles

Standard procedure for the alkylation of benzimidazole. 1-[3-(1H-benzo[d]imidazol-1-yl)propyl]-1H-benzo[d]imidazole. Benzimidazole (5.00 g, 42.3 mmol) was added slowly to sodium hydride (1.22 g, 50.8 mmol) in THF (350 ml). The mixture was stirred and refluxed for 1 h, and 1,3-dibromopropane (2.1 ml, 21.1 mmol) was added dropwise. The mixture was heated under reflux for a further 2 h. The salts formed were removed by filtration on a celite bed and the solution was evaporated to dryness to yield a tan solid which was purified by column chromatography using neutral alumina as absorbent with ethyl acetate/methanol as eluent to yield 1-[3-(1*H*-benzo[d]imidazol-1-yl)propyl]-1*H*-benzo[d]imidazole, as a white solid (5.14 g, 44%); mp 119-121 °C (lit.[29] mp 120-121 °C); δ_H 2.50-2.59 (2 H, m, 2'-CH_2), 4.18-4.24 (4 H, t, *J* 6.9, NCH_2), 7.28-7.35 (4 H, m, Ar-H), 7.84-7.88 (4 H, m, Ar-H), 8.10 (2 H, s, H-2).

1,3-Di(3-bromopropyl)-3H-benzo[d]imidazol-1-ium bromide. Using the standard procedure for the alkylation of benzimidazole, benzimidazole (1.00 g, 8.5 mmol), sodium hydride (0.25 g, 10.2 mmol) and 1,3-dibromopropane (8.6 ml, 84.6 mmol) gave 1,3-di(3-bromopropyl)-3*H*-benzo[d]imidazol-1-ium bromide, as a colourless solid (0.31 g, 10%); mp >300 °C (Found: M$^+$, 358.9758. $C_{13}H_{17}N_2Br_2$ requires M, 358.9758); δ_H 2.53-2.71 (4 H, m, 2'-CH_2), 3.50-3.70 (4 H, t, *J* 6.0, CH_2Br), 4.67-4.84 (4 H, t, *J* 7.0, NCH_2), 7.57-7.64 (2 H, m, Ar-H), 7.81-7.88 (2 H, m, Ar-H), 11.15 (1 H, s, Im-2-H); δ_C 29.94 (2'-CH_2), 32.35 (CH_2Br), 42.05 (NCH_2), 113.57, 113.62, 127.68, 127.83, 131.73, 131.86, 143.42 (C-2); *m/z* 361 (M, 37%), 317 (100), 271 (87), 235 (23), 208 (9) and 131 (11).

1-[3-(Phenylselanyl)propyl]-1H-benzimidazole **18**. Using the standard alkylation procedure for benzimidazoles, benzimidazole (2.00 g, 16.9 mmol) and 1-bromo-3-chloropropane (1.3 ml, 13.0 mmol) yielded 1-(3-chloropropyl)-1*H*-benzimidazole as an oil (1.80 g, 55%), (Found: M$^+$, 194.0614. $C_{10}H_{11}N_2Cl$ requires M, 194.0611); υ_{max}/cm^{-1} 1614, 1496, 1459, 1384, 1366, 1331, 1286, 1246, 1203, 767 and 745; δ_H 2.28-2.38 (2 H, m, 2'-CH_2), 3.46-3.51 (2 H, t, *J* 5.9, CH_2Cl), 4.40-4.45 (2 H, t, *J* 6.5, NCH_2), 7.27-7.36 (2 H, m, Ar-H), 7.43-7.47 (1 H, m, Ar-H), 7.82-7.85 (1 H, m, Ar-H) and 7.95 (1 H, s, Im-2-H); δ_C 32.50 (2'-CH_2), 41.60 (CH_2Cl), 41.96 (NCH_2), 109.86, 120.91, 122.75, 123.55, 134.00, 143.46 (C-2) and 144.21; *m/z* 194

(M+, 37%), 131 (100), 104 (14), 77 (23), 51 (9) and 39 (11). Diphenyl diselenide (0.500 g, 1.6 mmol) was dissolved in absolute ethanol (300 ml) at room temperature and sodium borohydride (0.132 g, 3.5 mmol) was added slowly to the stirred solution at 0 °C. The solution was stirred for a further 10 min at room temperature, and a solution of 1-(3-chloropropyl)-benzimidazole (0.623 g, 3.2 mmol) in absolute ethanol (50 ml) added. After stirring for 3 h at room temperature, the solution was evaporated to dryness, and 2 M hydrochloric acid solution (100 ml) added, and the acidic solution washed with light petroleum. The solution was basified to pH 8 with saturated sodium carbonate solution followed by the addition of 2 M sodium hydroxide solution until the aqueous solution was at pH 14. The hydroxide solution was extracted with dichloromethane, and the combined organic extracts dried and evaporated to dryness to yield 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18** as a yellow oil (0.617 g, 61%) which required no purification; (Found: M+, 316.0481. $C_{16}H_{16}N_2Se$ requires M, 316.0478); υ_{max}/cm^{-1} 1615, 1579, 1495, 1478, 1459, 1438, 1367, 1287, 1260, 1228 and 741; δ_H 2.17-2.29 (2 H, m, 2'-CH_2), 2.81-2.87 (2 H, t, *J* 6.8, PhSeCH_2), 4.29-4.35 (2 H, t, *J* 6.8, NCH_2), 7.28-7.39 (5 H, m, Ar-H), 7.47-7.49 (3 H, m, Ar-H), 7.79-7.81 (1 H, m, Ar-H), 7.84 (1 H, m, 2-H); δ_C 23.24, 28.62 ($SeCH_2$), 43.10 (NCH_2), 108.58, 119.47, 120.94, 121.16, 121.94, 128.00, 128.28, 131.86, 132.65, 141.95 and 142.92; *m/z* 316 (M+, 8%), 160 (38), 131 (100), 104 (7), 77 (25) and 51 (20).

Attempted radical cyclisation of 1-(3-phenylselanylpropyl)-1H-benzimidazole **18**. Using the standard radical cyclisation procedure, 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18** (0.600 g, 1.89 mmol) gave 2,3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazole **12a** (5%) and 1-propyl-1*H*-benzimidazole (89%); (Found: M+, 160.1000. $C_{10}H_{12}N_2$ requires M, 160.1000); υ_{max}/cm^{-1} 1615, 1498, 1459, 1384, 1287, 1259, 1213 and 743; δ_H 0.86-0.92 (3 H, t, *J* 7.3, CH_3), 1.77-1.92 (2 H, m, 2'-CH_2), 4.02-4.07 (2 H, t, *J* 7.0, NCH_2), 7.21-7.29 (2 H, m, Ar-H), 7.32-7.37 (1 H, m, Ar-H), 7.77-7.81 (1 H, m, Ar-H) and 7.82 (1 H, s, Im-2-H); δ_C 11.67 (CH_3), 23.47 (2'-CH_2), 47.03 (NCH_2), 109.89, 118.89, 120.67, 122.33, 123.90, 134.23, 143.36, 144.28; *m/z* 160 (M+, 66%), 131 (100), 118 (10), 104 (10) and 77 (22). The yields of products were determined by ^1H NMR spectroscopic analysis using 1,4-dimethoxybenzene as internal standard.

2-Deuterio-1-[3-(phenylselanyl)propyl]-1H-benzimidazole. Deuteriation at *C*-2 was achieved using the standard procedure for functionalisation at *C*-2. 1-(Triphenylmethyl)-benzimidazole (6.00 g, 16.5 mmol) and deuterium oxide (1.0 ml, 50.0 mmol) gave 2-deuterio-1-(triphenyl-methyl)benzimidazole. Without further purification the triphenylmethyl group was removed using the standard procedure for deprotection to yield crude 2-(deuterio)-1*H*-benzimidazole (1.19 g, 61% D measured by MS) as colourless crystals. The general procedure for the alkylation of benzimidazoles was followed; 2-(deuterio)-1*H*-benzimidazole (1.19 g, 10.0 mmol), sodium hydride (0.29 g, 12.0 mmol) and 1-iodo-3-(phenylselanyl)-propane (2.43 g, 7.5 mmol) gave 2-deuterio-1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole as a yellow oil (1.49 g, 47%, 61% D measured by MS) (Found: M+, 317.0541. $C_{16}H_{15}N_2DSe$ requires M, 317.0540); the ^1H and ^{13}C spectra were the same as those for **18**; *m/z* 317 (M+, 17%), 160 (30), 157 (27), 132 (100), 131 (42), 78 (31) and 77 (79).

Radical cyclisation of 2-deuterio-1-[3-(phenylselanyl)propyl]-1H-benzimidazole. Using the standard conditions for radical cyclisation, 2-deuterio-1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole, AIBN (0.268 g, 1.63 mmol) and 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **18**} (0.455 g, 61% deuterium) yielded an oil (0.189 g). Analysis by GCMS and ^1H NMR spectroscopy showed a mixture of 2-deuterio-1-propyl-2-benzimidazole (and 1-propyl-2-benzimidazole) (66%, analysis of the mass spectrum showed 60% deuterium on the benzimidazole moiety and <2% on the side chain) and 2,3-dihydro-1*H*-benzo[*d*]pyrrolo-[1,2-*a*]-imidazole **12a** (16%).

Radical cyclisation of 1-[3-(phenylselanyl)propyl]-1H-benzimidazole 17 using Bu_3SnD. Using the standard conditions for radical cyclisation, Bu_3SnD (1.04 ml, 3.91 mmol) and 1-[3-(phenylselanyl)propyl]-1*H*-benzimidazole **17** (1.030 g, 3.26 mmol) gave an oil (0.389 g). Analysis by GCMS and ^1H NMR spectroscopy showed a mixture of 1-(3-deuteriopropyl)-benzimidazole (and 1-propyl-2-benz-imidazole) (57%, analysis of the mass spectrum showed <5% deuterium on the benzimidazole moiety and *ca.* 90% on the side chain) and 2,3-dihydro-1*H*-benzo[*d*]pyrrolo-[1,2-*a*]-imidazole **12a** (17%).

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