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Radical Catalysed Cyclisations onto Sulfone-Substituted Indoles

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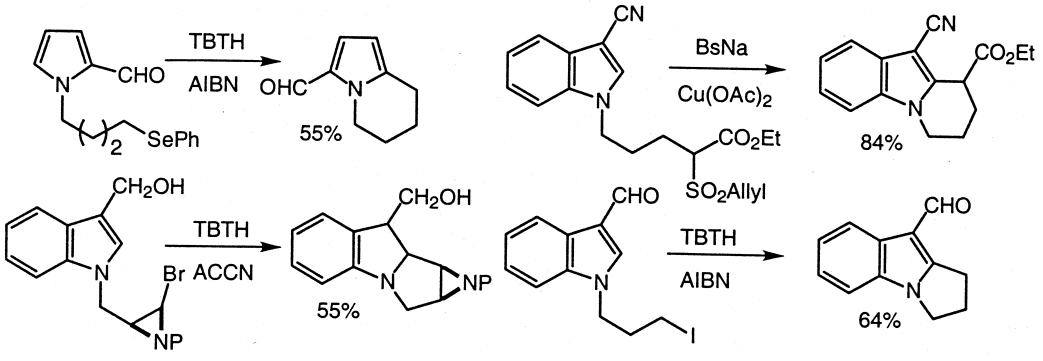
Abstract—A new radical chain process catalysed by sulfonyl radicals has been used for the synthesis of functionalised indoles.

Radical cyclisations have gained widespread appeal for synthetic chemistry and have been widely used in target-synthesis.[1] Of particular importance have been methods based on chain processes as they maintain a low concentration of radicals which is often important for devising selective and efficient methodologies.[2] In recent years radical cyclisations involving aromatic species have attracted considerable attention and in particular the cyclisation of σ-aryl radicals has been widely exploited as a general synthetic approach to polycyclic systems incorporating an aromatic ring. In the context of heterocyclic chemistry this has been nicely utilised by Jones and co-workers.[3] An alternative approach involves the addition of a radical species to an aromatic nucleus and there have been many examples of intramolecular radical addition reactions onto aromatic systems. These are often oxidative in nature resulting in the re-establishment of the aromatic nucleus.[4] In the context of the present work, it is relevant to draw attention to the cyclisations reported by the groups of Ziegler,[5] Moody,[6] Bowman[7] and Chuang[8] which demonstrate that substituted heterocycles can undergo radical cyclisations which can be accompanied by oxidation. Representative examples of such oxidative cyclisations are shown in Scheme 1 and are synthetically useful and mechanistically complex; it is clearly the case that further work is required in order to delineate their scope and limitations. It is also unclear which structural features are required in order to facilitate oxidation under TBTH conditions;[9] in which case the use of a chemical oxidant may be useful.[8] However, one can envisage circumstances under which regioselectivity cannot be assured and therefore there may be a case for developing alternative cyclisation protocols.

One possibility is to incorporate a group which will participate in *ipso*-substitution. The use of sulfur-based groups has served this purpose well and appears to offer a general strategy which is distinct from most oxidative radical cyclisations and which may offer some opportunities for regiocontrolled cyclisation. Recent work from the groups



Scheme 1. Oxidative radical cyclisations.

Keywords: radical cyclisation; sulfonyl radicals; indoles.
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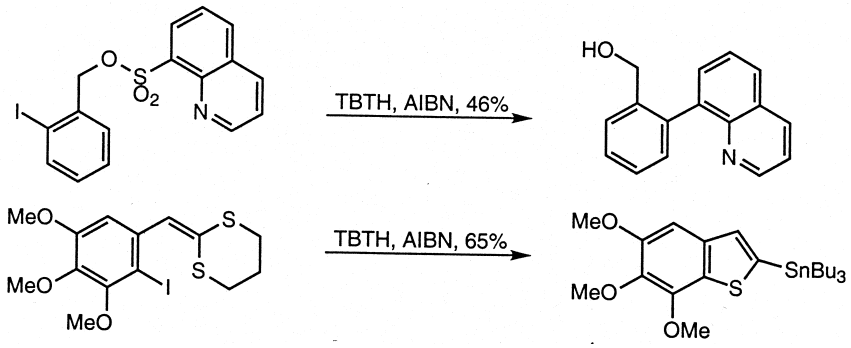


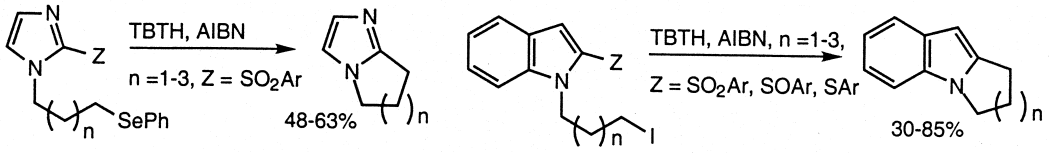
Scheme 2.

of Motherwell[10] and Harrowven[11] provide outstanding examples of *ipso*-substitution. In the former case the use of readily available sulfonates and sulfonamides ensures that this method can be readily applied to a wide range of examples. In the latter case the incorporation of such a transformation into the elaborate cascade is a powerful illustration of the potential of *ipso*-substitution protocols for synthesis (Scheme 2).

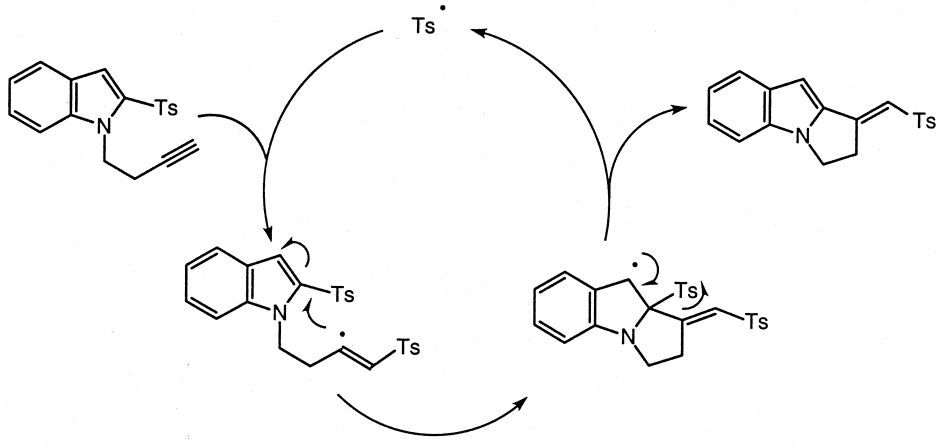
Our work in this area has focused on the development of new substitution reactions directed toward the synthesis of aromatic heterocyclic sulfones. In particular, we became interested in the synthesis of fused and substituted indole derivatives and our early finding that sulfonyl substituted indoles would participate in intermolecular radical substitution reactions[12,13] led us to examine intramolecular substitution reactions.[14,15] We and others have demonstrated that *ipso*-substitution can be an effective approach to polycyclic heterocycles. In addition to our own work,[16] Bowman[17] and Muchowski[18] have reported radical cyclisations of phenylsulfanyl, phenylsulfinyl and (most efficiently) phenylsulfonyl substituted nitrogen heterocycles as illustrated in Scheme 3.

The majority of these cyclisations are mediated using conventional (but rather toxic) tri-*n*-butyltin hydride methodology. Dissatisfied with the tin-mediated approach, we became interested in devising alternative chain processes without using TBTH and reasoned that β-sulfonylvinyl or alkyl radicals should undergo *ipso*-substitution under conditions which should operate under sub-stoichiometric (catalytic) conditions.[19] A generalised mechanistic principle is depicted in Scheme 4 and the prospect of devising methodology which would retain functionality in the product was an exciting added advantage of pursuing this type of strategy.[20]

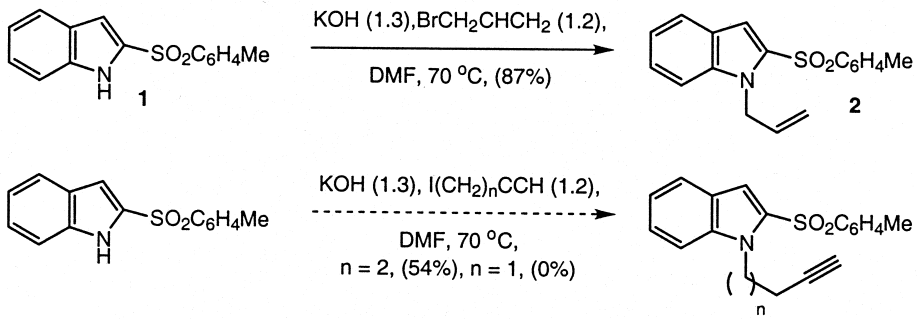
The purpose of this paper is to describe our work which demonstrates that this approach is feasible and delivers products in high yields.[21]



Scheme 3.



Scheme 4.



Scheme 5.

Synthesis of Precursors

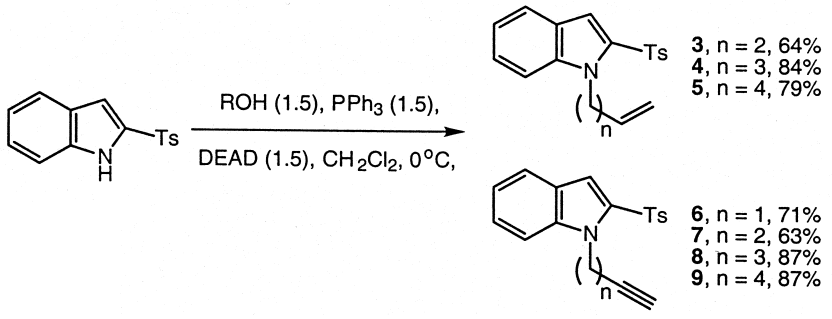
In order to prepare the precursors we made use of the starting material 2-*p*-toluenesulfonylindole **1** which was prepared using a slight modification of our previously described procedure. Initially we proposed to prepare precursors by simple acylation of 2-*p*-toluenesulfonylindole **1**, however, despite numerous attempts we were unable to effect acylation with 4-pentynoyl chloride. This is somewhat surprising given the ease with which indole participates in acylation protocols. Similarly surprising was our finding that *N*-alkylation of 2-*p*-toluenesulfonylindole **1** with alkyl iodides was variable and although such a procedure could be used for the preparation of **2** it was generally unsatisfactory for our studies (Scheme 5).

We assume that *N*-acylation or alkylation of 2-*p*-toluenesulfonylindole **1** is hindered due to reduced nucleophilicity in relation to indole and this may be an important feature of some sulfone-substituted heterocycles. In an attempt to devise a general method for the production of the appropriate alkenyl and alkynyl substrates we considered the use of Mitsunobu-type procedures. *N*-Alkylation of indoles using such methods are reported to be unsuccessful unless electron-withdrawing groups are present.[22] We believed that the powerful inductive effect of the sulfonyl group would enable us to use this type of reaction. We were able to show that this method can be used to prepare *N*-alkynyl and *N*-alkenyl derivatives of 2-*p*-toluenesulfonylindoles (Scheme 6). The mildness of the procedure, as illustrated by its compatibility with the terminal alkyne moiety, is notable. This methodology should be a useful general approach to the preparation of substrates of this type.

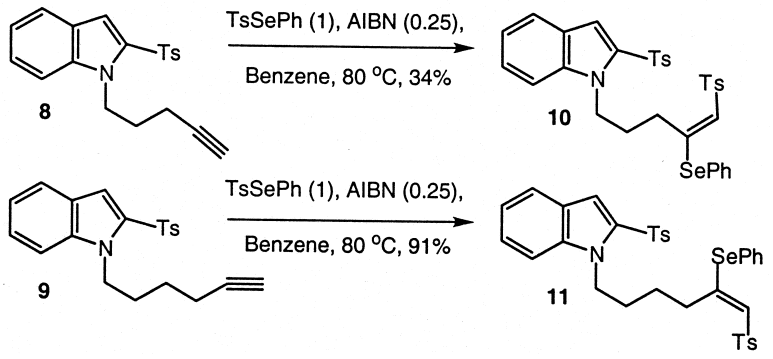
Cyclisation Studies

Our initial studies were directed towards promoting cyclisation of **7** using toluenesulfonyl bromide (1 equiv.), which we found to be unsuccessful leading to a complex mixture of products. We then decided to utilise the reagent widely used by Back and co-workers, Se-phenyl-*p*-tolueneselenosulfonate (TsSePh).[23] However, we found that treatment of either **8** or **9** with this reagent (1 equiv.) under radical chain conditions led to the addition products **10** and **11**, with no trace of the desired cyclisation. The proposed structures **10** and **11** are consistent with literature precedent; radical addition of TsSePh to alkynes is known to be a highly regio- and stereo-selective process.[24] Interestingly, subjection of alkyne **6** to similar reaction conditions for a prolonged period, led only to the isolation of starting material (95%). This result may reflect the relatively electron deficient nature of the alkyne moiety, which might be expected to exhibit slow reactivity with electrophilic toluenesulfonyl radicals (Scheme 7).

Encouraged by the prospect of using slow addition and dilution factors to enhance the possibility of obtaining the desired cyclisation products, we elected to study the cyclisation of **7** using sub-stoichiometric TsSePh. Initially these reactions were plagued by the formation of complex mixtures from which we were unable to isolate any of the desired products. However, after considerable experimentation, we were pleased to find that syringe-pump addition of TsSePh and AIBN to a solution of substrate **7** at 80°C in benzene led to the product **12** isolated in 72–89% yield. The *E*-stereochemistry of the product was confirmed by crystallography (Fig. 1) and the isolation of this particular product



Scheme 6.



Scheme 7.

is noteworthy in that the presence of the sulfonyl group would appear to maintain the 'diene character' of the product. Similar cyclisation was observed with alkyne **8** and gave the product **13** in 76–84% yield (Scheme 8). In contrast, and despite repeated attempts, we were unable to isolate the seven-membered ring product from cyclisation attempts using **9**; we isolated only the addition product **11**.

Our attention turned to cyclisation of *N*-alkenyl substrates and the results were generally analogous to the alkyne cases. Thus treatment of *N*-allyl-2-*p*-toluenesulfonylindole **2** led only to the isolation of starting material in good yield (92%). Treatment of **3** and **4** under analogous conditions gave the desired cyclisation products **14** and **15** in good yields (Scheme 9). However, attempted cyclisation of **5** led only to the isolation of selenide **16**, which could be optimised by increasing the quantity of TsSePh (1 equiv.).

Discussion

The results presented in this paper demonstrate that alkyl and vinyl radical cyclisations can be promoted without using tri-*n*-butyltin hydride (TBTH). These reactions can be carried out under what might loosely be defined as 'catalytic' conditions, although clearly TsSePh is not truly a catalyst in that it is not isolated unchanged at the end of the reaction. The reactions of the presumed β-sulfonyl alkyl radicals proceed in yields which are comparable to those we have obtained using the TBTH/alkyl iodide method, and would appear to offer considerable advantages in that the products incorporate a toluenesulfonyl moiety. It is particularly interesting to note the excellent conversions from cyclisations using the *N*-alkynyl substrates, particularly in view of the poor yields isolated from analogous vinyl halide/TBTH methodology previously reported by us.

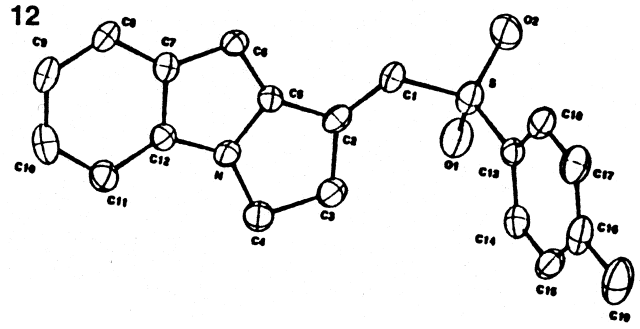
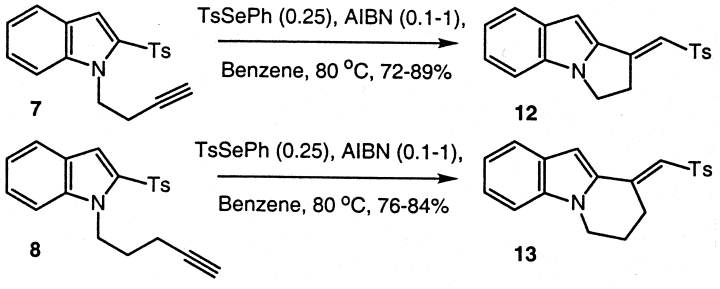
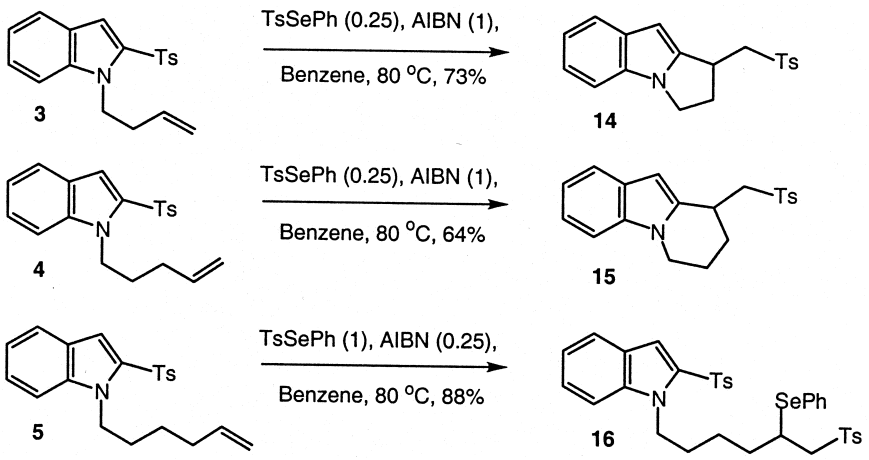


Figure 1.



Scheme 8.



Scheme 9.

In addition the products isolated from the reactions have the proposed indole structure as opposed to the pyrrolo structure and we presume that the observed tautomer is stabilised by conjugation of the 'diene' with the sulfonyl moiety. The chemistry of this new ring system may be of some synthetic utility in the production of functionalised indole derivatives.

It is interesting to note the lack of reactivity of the *N*-allyl and *N*-propargyl derivatives **2** and **6**, respectively, as they illustrate once again the electrophilicity of toluenesulfonyl radicals, a feature which, in our view, has not been fully exploited for synthetic gain. Moreover the failure of the method to deliver the seven-membered ring products contrasts at least with our previous work on alkyl radical cyclisations, in which we were able to prepare seven-membered rings using the alkyl iodide/TBTH methodology. One explanation for this is the relatively fast rate of phenylseleno group transfer to the alkyl or vinyl radical compared with cyclisation.

There has been considerable interest in radical cyclisation of heterocyclic derivatives and a number of groups have made mechanistic hypotheses. Most notably the work of Bowman and co-workers[17] appears to support our initial mechanistic proposal based on a radical chain process and we suggest that the results we have described in this paper can most readily be explained using the cycle described in Scheme 4. Thus, the toluenesulfonyl radical undergoes addition to the (relatively) electron rich alkene or alkyne to generate the intermediate β-sulfonyl-vinyl (or alkyl) radical, which then undergoes addition to generate the indoline radical. β-Scission gives the product and regenerates the chain carrier Ts radical. The success of these reactions using TsSePh (0.25 equiv.) and AIBN (0.1 equiv.) provides supporting evidence for such a catalytic cycle, although clearly a related electron transfer chain process cannot be ruled out. From an experimental viewpoint the optimal yields we have obtained have used additional portions of AIBN (usually to a maximum of 1 equiv.) but the improvement in yield is <10% and in our view this is mechanistically insignificant.

Conclusions

In conclusion we have shown that toluenesulfonyl radicals can be used to initiate a radical chain process for the synthesis of new classes of fused indoles which may be interesting from a synthetic and medicinal chemistry viewpoint. Moreover, we have shown that these non-tin methods can be used to promote cyclisations which are generally comparable or superior to those using TBTH methodology. It is likely that similar cyclisations will be successful with related heterocycles and the present work should facilitate further developments in this area.

Experimental

2-(Toluene-4-sulfonyl)-1*H*-indole 1. To a solution of indole (1.3 g, 11 mmol) in THF (40 ml) at −78°C was added dropwise *n*-BuLi (1.6 M in hexane, 7 ml, 11 mmol). The solution was allowed to stir for 30 min. CO_2 was then bubbled through the mixture until a constant pale yellow colour persisted (ca. 10 min). The reaction mixture was reduced in vacuo at 0°C to yield a white crystalline solid. This solid was redissolved in cold (~0°C) THF (50 ml), and the solution cooled to −78°C. *t*-BuLi (1.5M in hexane, 13 ml, 19 mmol) was added dropwise to the solution which was allowed to stir for a further 20 min. *p*-Toluenesulfonyl fluoride (1.9 g, 11 mmol) was added in a single portion and the solution allowed to warm to room temperature overnight. The mixture was poured onto an ice/brine slush (1:1, 100 ml). The mixture was extracted with ethyl acetate (2×100 ml), the combined organic fractions dried ($MgSO_4$), filtered and reduced in vacuo. The mixture was purified by flash column chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (1.79 g, 61%) as a white crystalline solid. Mp 196°C (Lit. 197°C); (ν_{max}/cm^{-1}: 3441 (N–H) 1320 and 1147 (SO_2); δ_H: 2.31 (s, 3H, Ar–CH_3) 7.07–7.11 (m, 2H, *H*3 and *H*5) 7.19 and 7.83 (*AA′BB′*, 4H. –SO_2Ar–*H*) 7.22–7.28 (m, 1H, *H*6) 7.33–7.36 (m, 1H, *H*7) 7.57–7.60 (m, 1H, *H*4);

9.1 (s,1H, N–*H*); δ_C: 22.03, 109.26, 112.73, 121.94, 123.05, 126.36, 127.49, 127.76, 130.41, 134.85, 137.47, 138.89, 144.98; HRMS (EI) $C_{15}H_{13}NO_2S$ requires 271.0667. Found 271.0667.

1-Allyl-2-(toluene-4-sulfonyl)-1*H*-indole 2. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.186 g, 0.67 mmol) and allyl bromide (0.18 ml, 0.249 g, 2.1 mmol) in DMF (4 ml) at room temperature, was added in a single portion potassium hydroxide (85 wt.%) (0.120 g, 2.1 mmol). The reaction mixture was stirred for four days, after which it was diluted with dichloromethane (20 ml) and washed with water (4×5 ml) and brine (5 ml); the combined organic fractions were dried ($MgSO_4$), filtered and reduced in vacuo. The residue was purified by flash chromatography (silica gel) [eluant—petrol/ether (gradient) 19:1, 9:1, 4:1,1:1] followed by recrystallisation (ether/petrol) to give the title compound (0.186 g, 87%) as a white crystalline solid. Mp 162°C; ν_{max}/cm^{-1}: 1319 and 1153 (SO_2); δ_H: 2.38 (s, 3H, Ar–C*H*$_3$) 4.73 and 4.93 (m, 2H, N–C*H*$_2$) 4.95–4.98 (m, 2H, –C=C*H*$_2$) 5.56–5.72 (m, 1H, N–CH$_2$C*H*=CH$_2$) 7.16–7.19 (m, 1H, *H*5) 7.23–7.37 (m, 3H, *H*3, *H*6 and *H*7) 7.23 and 7.80 (*AA′BB′*, 4H, –SO$_2$Ar–*H*) 7.67–7.71 (m, 1H, *H*4); δ_C: 22.04, 47.26, 111.41, 111.54, 117.35, 121.70, 123.27, 125.77, 126.12, 128.26, 130.27, 132.62, 135.30, 138.61, 139.41, 144.87; HRMS (EI) $C_{18}H_{17}NO_2S$ requires 311.0980. Found 311.0980.

1-But-3-enyl-2-(toluene-4-sulfonyl)-1*H*-indole 3. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.391 g, 1.4 mmol), triphenylphosphine (0.602 g, 2.3 mmol) and but-3-en-1-ol (0.20 ml, 0.239 g, 3.3 mmol) in dichloromethane (25 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.35 ml, 0.387 g, 2.2 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.297 g, 64%) as a white crystalline solid. Mp 79°C; ν_{max}/cm^{-1}: 1345 and 1154 (SO_2) 994 and 914 (CH=CH$_2$); δ_H: 2.19 (m, 2H, N–CH$_2$C*H*$_2$) 2.32 (s, 3H, Ar–C*H*$_3$) 4.26 (m, 2*H*, N–C*H*$_2$CH$_2$) 4.90–4.96 (m, 2H, CH=C*H*$_2$) 5.56–5.71 (m, 1H, C*H*=CH$_2$) 7.09 (m, 1H, *H*5) 7.20 (s, 1H, *H*3) 7.22–7.28 (m, 2H, *H*6 and *H*7) 7.22 and 7.76 (*AA′BB′*, 4H, SO$_2$Ar–*H*) 7.61 (m, 1H, *H*4); δ_C: 22.07, 34.55, 44.60, 111.17, 111.42, 117.90, 121.58, 123.37, 125.79, 126.07, 128.17, 130.39, 134.42, 135.16, 138.76, 139.14, 144.99; HRMS (EI) $C_{19}H_{19}NO_2S$ requires 325.1137. Found 325.1137.

1-Pent-4-enyl-2-(toluene-4-sulfonyl)-1*H*-indole 4. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.413 g, 1.5 mmol), triphenylphosphine (0.589 g, 2.3 mmol) and pent-4-en-1-ol (0.23 ml, 0.192 g, 2.2 mmol) in dichloromethane (25 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.35 ml, 0.387 g, 2.2 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.437 g, 84%) as a white crystalline solid. Mp 88°C; ν_{max}/cm^{-1}: 1350 and 1152 (SO_2) 992 and 915 (alkane) δ_H: 1.48–1.58 (m, 2H, N–CH$_2$C*H*$_2$CH$_2$) 1.94–2.0 (q, *J*=7.1 Hz, 2*H*, N–CH$_2$CH$_2$C*H*$_2$) 2.34 (s, 3H, Ar–C*H*$_3$) 4.16–4.22 (m, 2H, N–C*H*$_2$CH$_2$CH$_2$) 4.89–4.95 (m, 2H, CH=C*H*$_2$) 5.63–5.73 (m, 1H, C*H*=CH$_2$) 7.1–7.12 (m, 1H, *H*5) 7.22–7.29 (m, 3H, *H*3, *H*6 and *H*7) 7.23 and 7.76 (*AA′BB′*, 4H, SO$_2$Ar–*H*) 7.61–7.64 (m, 1H, *H*4); δ_C: 20.83, 27.94, 30.14, 43.59, 109.84, 110.04, 114.72, 120.28, 122.13, 124.54, 124.76, 126.96, 129.11, 133.97, 136.36, 137.53, 137.91, 143.72; HRMS (EI); $C_{20}H_{21}NO_2S$ requires 339.1293. Found 339.1293.

1-Hex-5-enyl-2-(toluene-4-sulfonyl)-1*H*-indole 5. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.420 g, 1.6 mmol), triphenylphosphine (0.604 g, 2.3 mmol) and hex-5-en-1-ol (0.27 ml, 0.225 g, 2.3 mmol) in dichloromethane (25 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.35 ml, 0.387 g, 2.2 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.431 g, 79%) as a white crystalline solid. Mp 100°C; ν_{max}/cm^{-1}: 1317 and 1153 (SO_2) 993 and 913 (CH=CH$_2$); δ_H: 1.3–1.4 (m, 2H, N–CH$_2$CH$_2$C*H*$_2$CH$_2$) 1.41–1.46 (m, 2H, N–CH$_2$C*H*$_2$CH$_2$CH$_2$) 1.88–1.95 (q, *J*=7.0 Hz, 2H, N–CH$_2$CH$_2$CH$_2$C*H*$_2$) 2.34 (s, 3H, Ar–C*H*$_3$) 4.17–4.22 (m, 2H, N–C*H*$_2$CH$_2$CH$_2$CH$_2$) 4.85–4.92 (m, 2H, CH=C*H*$_2$) 5.59–5.65 (m, 1H, C*H*=CH$_2$) 7.08–7.13 (m, 1H, *H*5) 7.19 (s, 1H, *H*3) 7.22–7.29 (m, 2H, *H*6 and *H*7) 7.23 and 7.76 (*AA′BB′*, 4H, SO$_2$Ar–*H*) 7.62 (m, 1H, *H*4); δ_C: 21.44, 25.93, 29.20, 33.14, 44.60, 110.50, 110.64, 114.73, 120.86, 122.74, 125.35, 125.68, 127.54, 129.72, 134.51, 137.95, 138.23, 138.53, 144.27; HRMS (EI) $C_{21}H_{23}NO_2S$ requires 353.1450. Found 353.1450.

1-Prop-2-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole 6. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.238 g, 0.88 mmol), triphenylphosphine (0.340 g, 1.3 mmol) and prop-2-yn-1-ol (0.08 ml, 0.077 g, 1.4 mmol) in dichloromethane (20 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.21 ml, 0.232 g, 1.3 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.193 g, 71%) as a white crystalline solid. Mp 122°C; ν_{max}/cm^{-1}: 3309 (CC–H) 1317 and 1154 (SO_2); δ_H: 2.00 (s, 1H, CC*H*) 2.32 (s, 3H, Ar–C*H*$_3$) 5.14–5.15 (d, *J*=2.1 Hz, 2H, N–C*H*$_2$) 7.12–7.18 (m, 1H, *H*5) 7.21 and 7.80 (*AA′BB′*, 4H, SO$_2$Ar–*H*) 7.27–7.39 (m, 2H, *H*3 and *H*6) 7.62–7.67 (m, 1H, *H*7) 7.68–7.69 (m, 1H, *H*4); δ_C: 22.05, 24.05, 34.09, 73.50, 111.23, 112.10, 122.16, 123.39, 125.93, 126.54, 128.25, 130.31, 134.92, 138.56, 139.12, 144.94; HRMS (EI); $C_{18}H_{15}NO_2S$ requires 309.0824. Found 309.0824.

1-But-3-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole 7. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (1.609 g, 5.9 mmol), triphenylphosphine (2.409 g, 9.2 mmol) and but-3-yn-1-ol (0.70 ml, 0.624 g, 8.9 mmol) in dichloromethane (100 ml) at 0°C was added dropwise diethyl azodicarboxylate (1.40 ml, 1.548 g, 8.9 mmol). The solution was allowed to warm to room temperature overnight,

then reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (1.209 g, 63%) as a white crystalline solid. Mp 110°C; ν_{max}/cm^{-1}: 3309 (CC–H) 1319 and 1154 (SO_2); δ_H: 2.16–2.17 (t, J=2.4 Hz, 1H, CC*H*) 2.56 (s, 3H, Ar–CH_3) 2.59 (m, 2H, N–CH_2CH_2) 4.59–4.64 (t, J=7.9 Hz, 2H, N–CH_2CH_2) 7.30–7.4 (m, 1H, *H*5) 7.45 and 7.98 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.46–7.52 (m, 2H, *H*3 and *H*6) 7.82–7.85 (d, 1H, *H*7) 7.88–7.91 (m, 1H, *H*4); δ_C: 20.29, 22.09, 24.05, 43.77, 71.31, 111.00, 111.74, 121.87, 123.40, 125.79, 126.27, 128.15, 130.51, 135.10, 138.46, 139.07, 145.17.; HRMS (EI) $C_{19}H_{17}NO_2S$ requires 323.0980. Found 323.0980.

1-Pent-4-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole 8. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.402 g, 1.5 mmol), triphenylphosphine (0.598 g, 2.3 mmol) and pent-4-yn-1-ol (0.20 ml, 0.181 g, 2.2 mmol) in dichloromethane (25 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.35 ml, 0.387 g, 2.2 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.433 g, 87%) as a white crystalline solid. Mp 96°C (Lit.[16] 93–95°C); ν_{max}/cm^{-1}: 3285 (CC–H) 1350 and 1152 (SO_2); δ_H: 1.71–1.79 (quint., J=7.3 Hz, 2H, $CH_2CH_2CH_2$) 1.99–2.12 (t, J=2.6 Hz, 1H, CC*H*) 2.12–2.18 (td, J=6.8 Hz, J'=2.6 Hz, 2H, CH_2CCH) 2.34 (s, 3H, Ar–CH_3) 4.3–4.35 (dd, J=8.7 Hz, J'=7.1 Hz, 2H, N–CH_2CH_2) 7.08–7.14 (m, 1H, *H*5) 7.23 (s, 1H, *H*3) 7.23 and 7.77 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.25–7.35 (m, 2H, *H*6 and *H*7) 7.62–7.63 (d, 1H, *H*4); δ_C: 15.69, 21.28, 28.03, 43.37, 69.16, 82.57, 110.21, 110.66, 120.85, 122.54, 124.94, 125.36, 127.38, 129.60, 134.40, 137.85, 138.46, 144.24; HRMS (EI) $C_{20}H_{19}NO_2S$ requires 337.1137. Found 337.1137.

1-Hex-5-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole 9. To a solution of 2-(toluene-4-sulfonyl)-1*H*-indole (0.415 g, 1.5 mmol), triphenylphosphine (0.597 g, 2.3 mmol) and hex-5-yn-1-ol (0.25 ml, 0.223 g, 2.3 mmol) in dichloromethane (25 ml) at 0°C was added dropwise diethyl azodicarboxylate (0.35 ml, 0.387 g, 2.2 mmol). The solution was allowed to warm to room temperature overnight. The solution was reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 14:3:3] to give the title compound (0.464 g, 87%) as a white crystalline solid. Mp 104°C; ν_{max}/cm^{-1}: 3295 (CC–H) 1347 and 1153 (SO_2); δ_H: 1.41–1.46 (m, 2H, N–$CH_2CH_2CH_2$) 1.58–1.6 (m, 2H, N–$CH_2CH_2CH_2$) 1.86–1.88 (t, J=2.5 Hz, 1H, CC*H*) 2.04–2.1 (td, J=6.9 Hz, J'=2.5 Hz, 2H, CH_2CCH) 2.34 (s, 3H, Ar–CH_3) 4.2–4.23 (t, J=7.8 Hz, 2H, N–$CH_2CH_2CH_2$) 7.1–7.18 (m, 1H, *H*5) 7.22 (s, 1H, *H*3) 7.23 and 7.76 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.24–7.28 (m, 2H, *H*6 and *H*7) 7.61–7.63 (m, 1H, *H*4); δ_C: 17.64, 21.28, 25.18, 28.58, 43.94, 68.41, 83.22, 110.24, 110.47, 120.66, 122.48, 124.90, 125.16, 127.24, 129.48, 134.25, 137.92, 138.25, 144.06; HRMS (EI) $C_{21}H_{21}NO_2S$ requires 351.1293. Found 351.1293.

1-[4-Phenylselanyl-5-(toluene-4-sulfonyl)-pent-4-enyl]-2-(toluene-4-sulfonyl)-1*H*-indole 10. A solution of 1-(pent-1-ynyl)-2-(toluene-4-sulfonyl)-1*H*-indole (0.100 g, 296 μmol), Se-phenyl-*p*-tolueneselenosulfonate (0.101 g, 325 μmol) and AIBN (0.013 g, 78 μmol) in benzene (12 ml) was stirred under reflux for 4 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.065 g, 34%) as a white crystalline solid. Mp 86°C; ν_{max}/cm^{-1}: 1318 and 1120 (SO_2); δ_H: 1.91 (m 2H, N–$CH_2CH_2CH_2$) 2.40 (s, 3H, Ar–CH_3) 2.41 (s, 3H, Ar–CH_3) 2.85 (m, 2H, N–$CH_2CH_2CH_2$) 4.36 (t, J=7.9 Hz, 2H, N–$CH_2CH_2CH_2$) 5.84 (s, 1H, C(Ts)*H*) 7.24–7.92 (m, 18H, Ar–**H**); δ_C: 22.07, 22.13, 30.44, 30.58, 44.40, 111.30, 111.36, 121.66, 123.31, 124.66, 125.81, 125.95, 126.23, 127.36, 128.21, 129.90, 130.38, 130.55, 130.62, 135.18, 137.09, 138.70, 139.17, 139.51, 144.58, 145.01, 159.43; HRMS (EI) $C_{33}H_{31}NO_4S_2Se$ requires 649.0860. Found 649.0900.

1-[5-Phenylselanyl-6-(toluene-4-sulfonyl)-hex-5-enyl]-2-(toluene-4-sulfonyl)-1*H*-indole 11. A solution of 1-hex-5-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole, (0.104 g, 296 μmol), Se-phenyl-*p*-tolueneselenosulfonate (0.101 g, 325 μmol) and AIBN (0.013 g, 78 μmol) in benzene (12 ml) was stirred under reflux for 4 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.178 g, 91%) as a white crystalline solid. Mp 89°C; ν_{max}/cm^{-1}: 1348 and 1151 (SO_2); δ_H: 1.61–1.69 (m, 4H, CH_2CH_2) 2.44 (s, 3H, Ar–CH_2) 2.46 (s, 3H, Ar–CH_3) 2.83–2.88 (t, J=7.2 Hz, 2H, CH_2C(SePh)) 4.30–4.35 (t, J=7.9 Hz, 2H, N–CH_2CH_2) 5.91 (s, 1H, C(Ts)*H*) 7.24–7.92 (m, 18H, Ar–*H*); δ_C: 22.03, 22.09, 27.69, 29.73, 32.87, 44.86, 111.15, 111.23, 121.56, 123.35, 124.57, 125.80, 126.06, 127.30, 128.13, 130.25, 130.48, 130.58, 135.21, 137.05, 138.77, 139.09, 139.70, 144.45, 145.01, 160.62; HRMS (EI) $C_{34}H_{33}NO_4S_2Se$ requires 663.1016. Found 663.1016.

1-(Toluene-4-sulfonylmethylene)-2,3-dihydro-1H-3*a*-aza-cyclopenta[*a*]indene 12. To a solution of 1-but-3-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole, (0.385 g, 1.2 mmol) in benzene (50 ml) under reflux was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenese-lenosulfonate (0.093 g, 298 μmol) and AIBN (0.198 g, 1.2 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.342 g, 89%) as a white crystalline solid. Mp 195°C; ν_{max}/cm^{-1}: 2255, 1623 (C=C), 1345 and 1146 (SO_2); δ_H: 2.49 (s, 3H, Ar–CH_3) 3.85–3.89 (m, 2H, N–CH_2CH_2) 4.24–4.29 (t, J=6.4 Hz, 2H, N–CH_2CH_2) 6.68 (s, 1H, C=C*H*Ts) 6.74 (s, 1H, *H*3) 7.14–7.19 (m, 1H, *H*5) 7.24–7.34 (m, 2H, *H*6 and *H*7) 7.41 and 7.91 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.67–7.9 (m, 1H, *H*4); δ_C: 20.52, 31.68, 41.42, 94.53, 109.13, 117.34, 119.70, 121.21, 122.36, 126.06, 128.81, 131.55, 133.10, 138.07, 138.59, 143.14, 144.32; HRMS (EI); $C_{19}H_{17}NO_2S$ requires 323.0980. Found 323.0980.

9-(Toluene-4-sulfonylmethylene)-6,7,8,9-tetrahydropyrido[1,2-*a*]indole 13. To a solution of 1-pent-4-ynyl-2-(toluene-4-sulfonyl)-1*H*-indole, (0.20 g, 0.59 mmol) in benzene (17 ml) under reflux was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenesselenosulfonate (0.046 g, 0.15 mmol) and AIBN (0.099 g, 0.59 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.167 g, 84%) as a white crystalline solid. Mp 151°C; ν_{max}/cm^{-1}: 2943, 1595 (C=C), 1324 and 1143 (SO_2); δ_H: 1.97–2.03; (quint., J=6.0 Hz, 2H, N–$CH_2CH_2CH_2$) 2.30 (s, 3H, Ar–CH_3) 3.01–3.05 (t, J=6.2 Hz, 2H, N–$CH_2CH_2CH_2$) 3.93–3.97 (t, J=5.9 Hz, 2H, N–$CH_2CH_2CH_2$) 6.72 (s, 1H, C=CHTs) 6.75 (s, 1H, *H*3) 7.10–7.15 (m, 1H, *H*5) 7.19–7.29 (m, 2H, *H*6 and *H*7) 7.34 and 7.85 (*AA′BB′*,4H, SO_2Ar–*H*) 7.43–7.46 (d, 1H, *H*4); δ_C: 22.06, 22.80, 24.48, 42.00, 101.00, 109.82, 121.30, 121.96, 122.03, 124.04, 127.56, 127.60, 130.31, 132.74, 137.91, 140.04, 144.08, 144.51; HRMS (EI) $C_{20}H_{19}NO_2S$ requires 337.1137. Found 337.1137.

1-(Toluene-4-sulfonylmethyl)-2,3-dihydro-1H-3*a*-azacyclopenta[*a*]indene 14. To a solution of 1-but-3-enyl-2-(toluene-4-sulfonyl)-1*H*-indole (0.215 g, 0.66 mmol) in benzene (17 ml) under reflux was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenesselenosulfonate (0.051 g, 0.17 mmol) and AIBN (0.110 g, 0.66 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. To the resultant reaction mixture was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenesselenosulfonate (0.020 g, 64 μmol) and AIBN (0.053 g, 0.32 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.156 g, 73%) as a white crystalline solid. Mp 192°C; ν_{max}/cm^{-1}: 1597 (Aromatic), 1338 and 1144 (SO_2); δ_H: 2.39; (s, 3H, Ar–CH_3) 2.40–2.48 (m, 1H, C*H*CH_2Ts) 2.81–2.89 (m, 1H, N–CH_2CH_2CH) 3.14–3.22 (dd, J=14.1 Hz, J'=10.0 Hz, 1H, N–CH_2CH_2) 3.53–3.59 (dd, J=14.1 Hz, J'=3.6 Hz, 1H, N–CH_2CH_2) 3.70–3.76 (m, 1H, N–CH_2CH_2CH) 3.87–3.95 (m, 1H, CHCH_2Ts) 4.03–4.10 (m, 1H, CHCH_2Ts) 6.03 (s, 1H, *H*3) 6.95–7.0 (m, 1H, *H*5) 7.06–7.08 (m, 1H, *H*6) 7.13–7.17 (m, 1H, *H*7) 7.32 and 7.78 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.42–7.45 (m, 1H, *H*4); δ_C: 19.75, 30.33, 32.80, 41.09, 58.27, 90.97, 107.58, 117.55, 118.82, 119.08, 126.10, 128.20, 130.65, 130.70, 134.40, 142.18, 143.17; HRMS (EI) $C_{19}H_{19}NO_2S$ requires 325.1137. Found 325.1137.

9-(Toluene-4-sulfonylmethyl)-6,7,8,9-tetrahydropyrido-[1,2-*a*]indole 15. To a solution of 1-pent-1-enyl-2-(toluene-4-sulfonyl)-1*H*-indole, (0.173 g, 0.51 mmol) in benzene (15 ml) under reflux was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenesselenosulfonate (0.040 g, 0.13 mmol) and AIBN (0.085 g, 0.51 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. To the resultant reaction mixture was added, via syringe pump [flow rate=1.78 ml h], a solution of Se-phenyl-*p*-toluenesselenosulfonate (0.017 g, 55 μmol) and AIBN (0.070 g, 0.42 mmol) in benzene (5 ml). Once the addition was complete, the mixture was stirred under reflux for another 6 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.110 g, 64%) as a white crystalline solid. Mp 153°C; ν_{max}/cm^{-1}: 2254, 1597 (Aromatic), 1315 and 1151 (SO_2); δ_H: 1.82–1.88 (m, 1H) 2.09–2.13 (m, 1H) 2.25–2.30 (m, 1H) 2.47–2.59 (m, 1H) 2.54 (s, 3H, Ar–CH_3) 3.37–3.45 (m, 1H) 3.71–3.76 (m, 2H) 3.93–4.02 (m, 1H) 4.18–4.24 (m, 1H) 6.20 (s, 1H, *H*3) 7.12–7.2 (m, 1H, *H*5) 7.23–7.3 (m, 1H, *H*6) 7.33–7.39 (m, 1H, *H*7) 7.45 and 7.96 (*AA′BB′*, 4H, SO_2Ar–*H*) 7.54–7.57 (m, 1H, *H*4); δ_C: 22.11, 22.38, 27.55, 30.89, 42.50, 61.51, 98.05, 109.30, 120.42, 121.54, 128.05, 128.33, 130.53, 131.19, 136.78, 137.22, 137.75, 145.37; HRMS (EI) $C_{20}H_{21}NO_2S$ requires 339.1293. Found 339.1293.

1-[5-Phenylselanyl-6-(toluene-4-sulfonyl)-hexyl]-2-(toluene-4-sulfonyl)-1*H*-indole 16. A solution of 1-hex-5-enyl-2-(toluene-4-sulfonyl)-1*H*-indole (0.153 g, 0.43 mmol), Se-phenyl-*p*-toluenesselenosulfonate (0.135 g, 0.43 mmol) and AIBN (0.018 g, 0.11 mmol) in benzene (20 ml) was stirred under reflux for 19 h. The solution was allowed to cool to room temperature, reduced in vacuo and the residue purified by flash chromatography (silica gel) [eluant—petrol/dichloromethane/ethyl acetate (gradient) 18:1:1, 8:1:1, 4:1:1] to give the title compound (0.253 g, 88%) as a white crystalline solid. Mp 81°C; ν_{max}/cm^{-1}: 1597 (Aromatic) 1317 and 1152cm (SO_2); δ_H: 1.36–1.56 (m, 6H, $CH_2CH_2CH_2$) 1.90–2.00 (m, 1H, C*H*(SePh)) 2.34 (s, 6H, 2×Ar–CH_3) 3.23–3.28 (m, 2H, CH_2(Ts)) 4.18–4.24 (m, 2H, N–CH_2CH_2) 7.11–7.81 (m, 18H, Ar–*H*); δ_C: 22.74, 25.87, 30.38, 34.14, 38.08, 45.69, 62.75, 111.77, 111.90, 122.19, 124.01, 126.43, 126.71, 128.79, 128.91, 129.35, 130.46, 131.07, 131.12, 135.84, 136.10, 139.38, 139.75, 145.72, 145.92; HRMS (EI) $C_{34}H_{35}NO_4S_2Se$ requires 665.1173. Found 665.1173.

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