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Palladium catalysed tandem cyclisation–anion capture processes. Part 8 [1]: In situ and preformed organostannanes. Carbamyl chlorides and other starter species

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Abstract

A sequential one-pot process is reported involving in situ, palladium catalysed, formation of a series of tributylstannyl-1,2-carbo and heterocyclic dialkylidene-5-membered rings from the corresponding 1,6-diynes and Bu_3SnH. These substrates and other organostannanes are then combined with carbamyl chlorides and iodobenzenes containing proximate alkene and alkynyl groups in palladium catalysed cyclisation–anion capture cascades affording a diverse range of heterocycles in good yield.

Keywords: Cascade; Carbamyl chlorides; Organostannanes; Tributyltinhydride

1. Introduction

Cascade ring forming processes via multiple insertions with concomitant introduction of functionally by replacing the β-hydride elimination step of a Heck reaction with a group or atom transfer offer wide ranging opportunities for substantially leveraging molecular complexity and diversity. This concept has been developed into powerful, widely applicable, highly regio- and stereo-selective palladium catalysed cyclisation–anion capture methodology [2,3]. The use of word 'anion' for the group or atom transfer/capture embraces both ionic and covalent sources of Y (Table 1) and is felt to be more appropriate than cross-coupling. Table 1 summarises the basic process which comprises four segments.

The starter species is usually an appropriate halide (Cl, Br, I) or triflate in which case the cascade begins with an oxidative addition reaction between the starter or "zipper" species and Pd(0) to generate an organopalladium(II) species. In monocyclisations the organopalladium(II) species cyclises onto the terminating species (T). Exchange of halide or triflate with the anion capture agent Y followed by reductive elimination generates a regiospecifically functionalised monocyclic product and regenerates Pd(0). In polycyclisation processes, the initial Pd(II) intermediate engages one or more relay species (R) before passing to the terminating phase and anion capture.

Aryl iodides [3,4], allyl, benzyl halides/acetates [5], vinyl halides/triflates [6], and propargyl halides/carbonate [7] have been successfully utilised as starter species in the palladium catalysed cyclisation–anion capture processes.

2. Results and discussion

In this paper, we describe the full detail of a new starter species, carbamyl chlorides, and their monocyclisation–anion capture processes [1,2] together with palladium

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Table 1
Potential combinations for (poly) cyclisation–anion capture processes

Starter species	Relay species (R)	Terminating species (T)	Y
Allyl	Alkene	Alkene	Anionic: H,CN, N_3, TsNR, SO_2Ph, $CH(CO_2R)_2$, enolates
Alkyl	Alkyne	Alkyne	
Vinyl	1,2-Diene	1,2-Diene	Neutral: amines, MeOH/CO, acrylates, allenes
Allenyl	1,3-Diene	1,3-Diene	
Carbamyl			Organometallics: RM [M = Sn(IV), B(III), Zn(II)]
Oxycarbonyl			

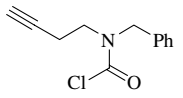
catalysed cyclisation–anion capture with in situ generated tributylstannyl 1,2-dialkylidenecyclopentanes anion capture agents.

2.1. Carbamyl chloride starter species

Initially, we prepared 5-membered and 6-membered cyclisation substrates containing an alkyne terminating species. Thus, **1a**,**1b** were prepared via reductive amination of 2-iodoaniline with benzaldehyde or aniline with 2-iodobenzaldehyde [8]. Treatment of **1a**,**b** with trimethylsilylacetylene under Sonogashira's conditions [9] afforded the desired TMS protected ethynyl derivatives **2a**,**b** in high yield. Deprotection with TBAF [10] afforded **3a**,**b** in 89–91% yield which were converted to the desired carbamyl chloride products **4a**,**b** on treatment with phosgene [11] in toluene at 0 °C (Scheme 1).

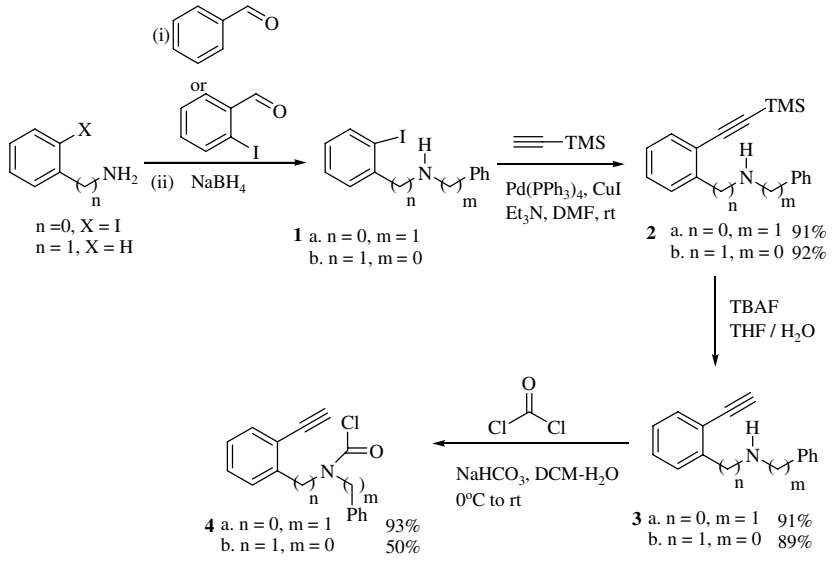
The carbamyl chlorides **4a**,**b** both contains benzene rings directly attached to the unsaturated group. We also made a carbamyl chloride in which the alkyne is attached to an alkyl chain. Thus, **5** was readily synthesised from *N*-benzyl-*N*-3-butynyl amine and phosgene by the method mentioned above.

A substrate containing a double bond was easily accessible from commercially available 2-isopropenylaniline (Scheme 2). Thus, reductive amination of 2-isopropenylaniline with benzaldehyde gave **6** and carbamyl chloride formation with phosgene gave **7** in good yield.

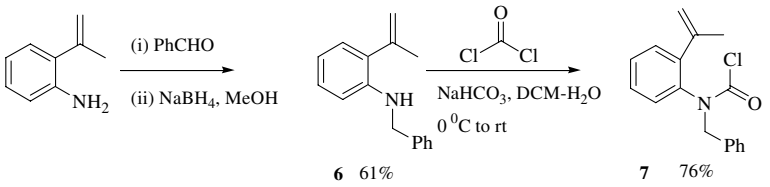


5

Catalytic cyclisation–anion capture of the carbamyl chlorides was studied using tributylstannanes and a catalyst system consisting of $Pd(OAc)_2$ (10 mol%) and tri-2-furylphosphane TFP (20 mol%) in toluene at 50 °C. Initially, we assessed cyclisation onto proximate alkynes to form *Z*-methylene oxindoles. The *E*- and *Z*-3-alkylideneoxindole moieties are found in many tyrosine kinase inhibitors [12], cyclin-dependent protein kinase inhibitors [13] and antirheumatic compounds [14]. When **4a** (1 mmol) was treated with tributylphenylethynyltin (1.1 mmol), $Pd(OAc)_2$ (10 mol%) and TFP (20 mol%) in toluene at 50 °C for 5 min the cyclisation–anion capture product **8** was obtained in 81% yield (Table 2, entry 1). A similar result was obtained when **4a** was reacted with 2-thienyltributylstannane (Table 2, entry 2). In this case oxindole **9** was formed in excellent yield and repetition of this reaction employing 1 mol% catalyst gave the product in 91% yield indicating that further reductions in catalyst loading

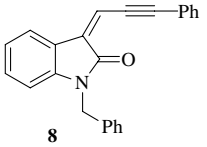
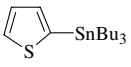
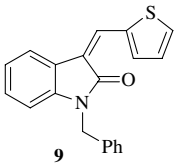
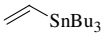
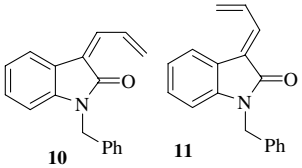
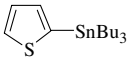
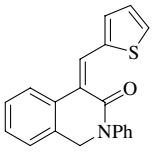
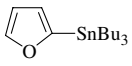
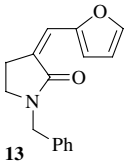
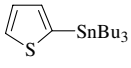
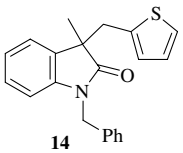
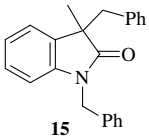


Scheme 1.

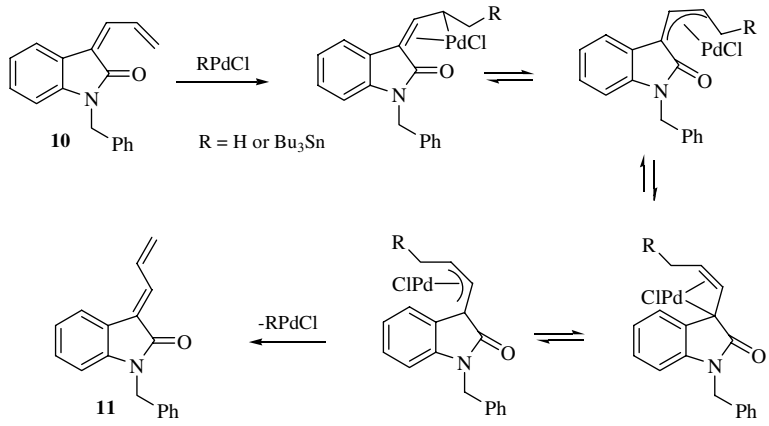


Scheme 2.

Table 2
Cyclisation–anion capture processes of carbamyl chlorides[a]

Entry	Carbamyl chloride	R–M	Product	Yield (%)[b]
1	**4a**	Ph—≡—$SnBu_3$	 **8**	81
2	**4a**		 **9**	88
3	**4a**		 **10** **11** 4 : 3	76
4	**4b**		 **12**	87
5	**5**		 **13**	60
6	**7**		 **14**	84
7	**7**	$PhB(OH)_2$	 **15**	50

[a] Reactions were carried out in toluene at 50 °C with carbamyl chloride (1 mmol) and organotin (1.1 mmol). Catalyst system: 10 mol% $Pd(OAc)_2$ and 20 mol% TFP.
[b] Isolated yield.



Scheme 3.

are possible. Treatment of **4a** with tributyl(vinyl)tin, $Pd(OAc)_2$ (10 mol%) and TFP (20 mol%) in toluene at 50 °C for 5 min afforded a mixture of geometrical isomers **10** and **11** in a 4:3 ratio (Table 2, entry 3). Isomerisation of **10** to **11** may occur via π-allyl palladium intermediates (Scheme 3) [15].

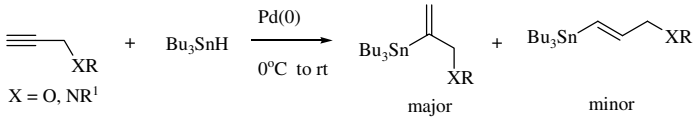
We also briefly studied the cyclisation–anion capture of **4b**. Thus, **4b** was reacted with 2-thienyl-tributylstannane under essentially same conditions as above affording isoquinolinone **12** in 87% yield (Table 2, entry 4). This demonstrates that 6-ring and 5-ring closure occur very rapidly at 50 °C and that cyclisation is unlikely to be the rate determining step in these reactions. In the event of cyclisation occurring at a similar rate to direct capture then significant amounts of direct capture byproduct would be isolated. We have not detected any such byproduct in the above processes. Compound **5** was also successfully employed in the cyclisation–anion capture processes (Table 2, entry 5). Initially, on treatment of **5** with $Pd(OAc)_2$, TFP and tributyl(2-furyl)tin in toluene at 50 °C, a low yield of product **13** was obtained (35%). However on changing the ligand, to tris-*t*-butylphosphane and the solvent to THF we found that the reaction proceeded in 60% yield over 48 h at room temperature. Such ligands promote oxidative addition to the acyl chlorine bond by increasing the nucleophilic nature of Pd(0) and also favour the reductive elimination step [16]. Others have recently reported a closely related process affording α-alkylidene-β-lactams [17].

We also explored the cyclisation–anion capture processes of **7**. Thus, cyclisation onto the isopropenyl group of **7** to form **14** (Table 2, entry 6) is much slower (4 h), but proceeds in excellent yield (84%). The use of phenyl boronic acid as anion capture reagent [18] resulted in **15** in 50% yield (Table 2, entry 7). This reaction was considerably slower (50 h, 90 °C) than those involving organostannane anion capture reagents. The carbamyl chloride cyclisation onto proximate alkynes was, as expected, regio- and stereo-selective and results in the formation of two new bonds and one ring in these cases. In all cases the processes employing organo tributylstannanes proceeded in excellent yield.

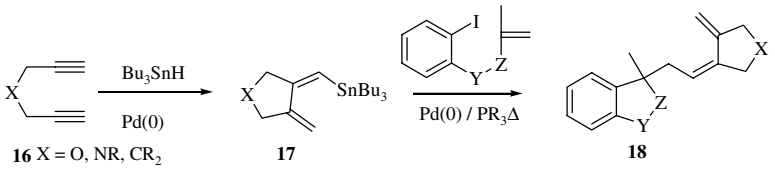
2.2. In situ generated anion capture agents

The basic strategy makes use of the known regio-selective palladium catalysed hydrostannylation of terminal alkynes bearing a β- or γ-heteroatom (Scheme 4) [19]. This strategy has proved extremely powerful in generating complex organotin(IV) anion capture species in situ via regio-selective hydrostannylation of appropriate alkynes as part of a temperature controlled cyclisation–anion capture cascade [20–22]. Following the success of the palladium catalysed cyclisation–anion capture with in situ generated vinylstannanes, we decided to investigate anion capture with in situ generated tributylstannyl 1,2-dialkylidenecyclopentanes.

Our synthetic plan focused on generating **17** in situ from **16** followed by the addition of an appropriate zipper and subsequent heating to trigger the cyclisation–anion capture cascade process to furnish **18** (Scheme 5). Recently, Lautens et al. [23] reported a new catalytic approach to the synthesis **16** using palladium. They found upon treatment of a wide range of terminal 1,6-diynes **16** with Bu_3SnH in the presence of $Pd(OH)_2/C$ (Pearlmans catalyst) triggered a hydrostannylation/cyclisation



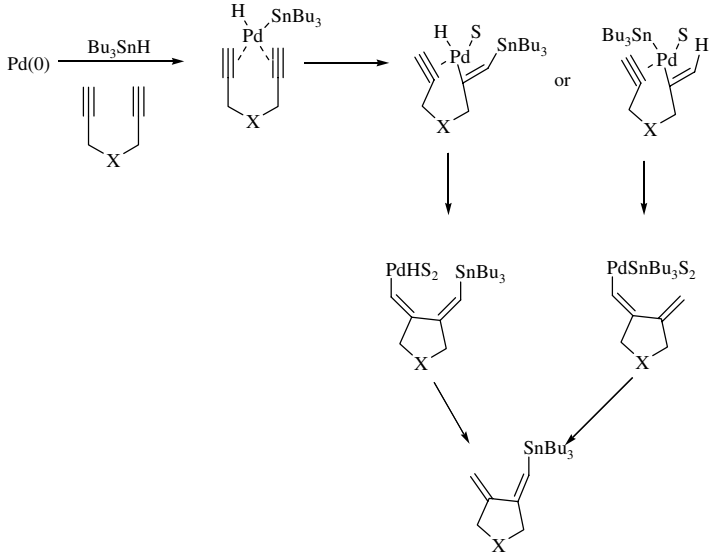
Scheme 4.



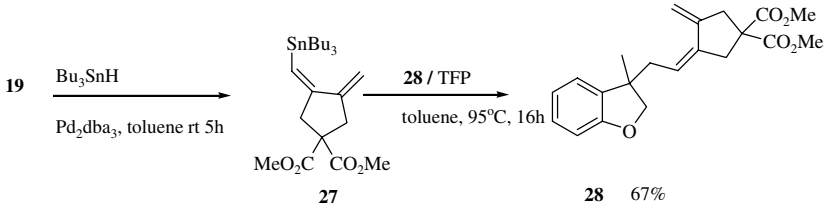
Scheme 5.

sequence generating **17** in excellent yield. They further showed that addition of triphenylphosphane retarded the reaction and that slow addition of Bu_3SnH was necessary to obtained a good yield of **17**. Transition metals are known to catalyse the decomposition of Bu_3SnH to Bu_6Sn_2 and H_2 [24] and this side reaction can be prevented by slow addition of Bu_3SnH via a syringe pump. A possible catalytic cycle for the synthesis of **17** is illustrated in Scheme 6 [23].

1,6-Diynes **19**–**22** were prepared in high yield using a standard alkylation procedure [25]. We selected **23**–**26** as cyclisation precursors (''zippers'') [18] generating 5-membered and 6-membered products. Initially 1,6-diyne **19** was reacted with Bu_3SnH, added via a syringe pump over 90 min, in the presence of tris(dibenzylideneacetone)dipalladium in THF at room temperature. After 2.5 h, the reaction mixture was examined using ^1H NMR spectroscopy and the exclusive formation of the tributylstannyl dialkylidenecyclopentane was confirmed. The presence of 3 singlets at δ 4.9, 5.2 and 5.8 corresponding to the olefinic protons clearly indicated the formation of **27**. THF was then removed after the initial hydrostannylation/cyclisation and Aryl iodide **23** and tris-2-furyl phosphane were then added and the mixture heated to 95 °C in toluene for 16 h to furnish **28** in 67% yield (Scheme 7). Having established the conditions for the cyclisation–anion capture processes, a series of cascade reactions were performed involving aryl iodides **24**, **25** and carbocyclic 1,6-diyne **19**. Aryl iodides cyclised efficiently with the capture of tributylstannyl dialkylidenecyclopentane derivative generated in situ from **19** to give the corresponding products **29**, **30** in 64–70% yield (Table 3, entries 2 and 3). The hydrostannylation/cyclisation of **20** followed by reaction with aryl iodides **23**–**26**

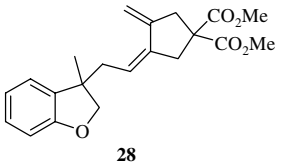
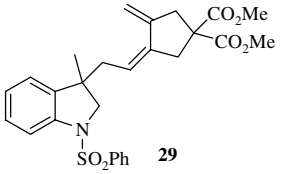
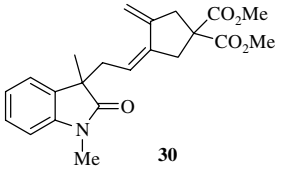
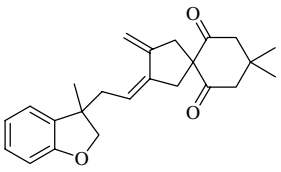
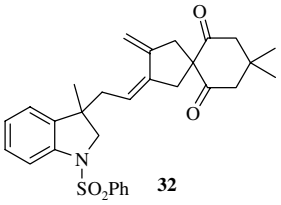
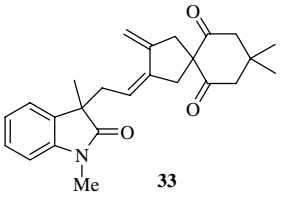
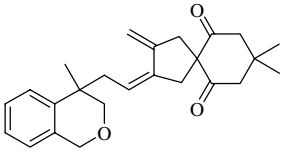


Scheme 6.



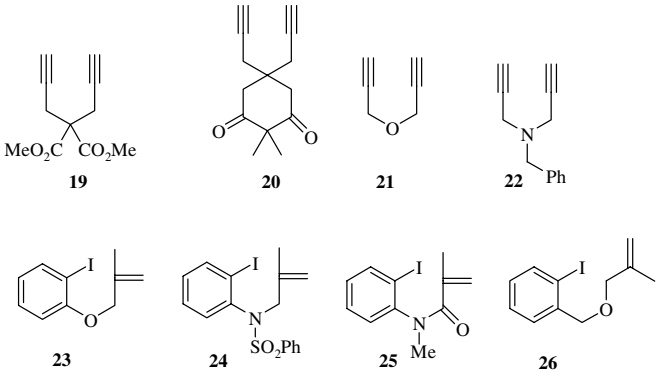
Scheme 7.

Table 3
Cyclisation–anion capture with in situ generated carbocyclic organostannanes

Entry	Aryl iodide	1,6-Diyne	Product	Yield (%)[a]
1	**23**	**19**	 **28**	67
2	**24**	**19**	 **29**	64
3	**25**	**19**	 **30**	70
4	**23**	**20**	 **31**	70
5	**24**	**20**	 **32**	62
6	**25**	**20**	 **33**	72
7	**26**	**20**	 **34**	62

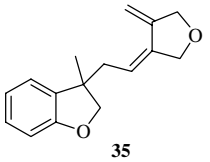
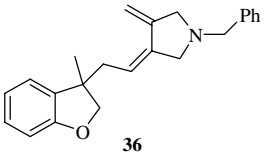
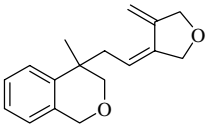
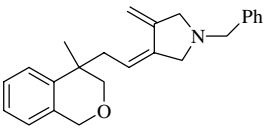
[a] Isolated yield.

gave the corresponding products **31**–**34** in 62–72% yield (Table 3, entries 4–7). Overall this protocol results in the formation of two new rings (5,5 and 6,5), two new C–C bonds and one stereocentre.



We next turned our attention to 1,6-diynes bearing a nitrogen or oxygen atom in the 4-position. Diynes **21** and **22** underwent clean hydrostannylation/cyclisation with the exclusive formation of the corresponding cyclised tributylstannyl derivatives as determined by ^{1}H NMR spectroscopy. Moderate to good yields of products were obtained when the resulting tributylstannyldialkylidene tetrahydrofuran (Table 4, entries 1 and 3) and pyrrolidine (Table 4, entries 2 and 4) were incorporated into the cascade process.

Table 4
Cyclisation–anion capture with in situ generated herterocyclic organostannanes

Entry	Aryl iodide	1,6-Diyne	Product	Yield (%)[a]
1	**23**	**21**	 **35**	62
2	**23**	**22**	 **36**	62
3	**26**	**21**	 **37**	62
4	**26**	**22**	 **38**	70

[a] Isolated yield.

3. Summary

We have developed a powerful palladium catalysed cyclisation–anion capture processes affording 3,3-disubstituted and *Z*-3-methyleneoxindoles, and heterocyclic1,3-dienes. The reactions occur in good yield and afford products with functionality offering considerable further synthetic opportunities such as Michael additions and cycloadditions.

4. Experimental

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Mass spectral data were obtained from a VG Autospec instrument operating at 70 eV (EI and FAB) or ZD 2000 electrospray instrument (ES). Accurate molecular masses were obtained from the EPSRC Swansea Mass Spectroscopy service using perfluorotributylamine or polyethylenimine as an internal standard. Microanalyses were obtained using a Carbo Erba MOD11016 instrument. IR spectra were determined on a Nicolet Magna FT-IR 560 spectrometer. The IR samples were prepared as thin films by evaporation of a solution of the compound in DCM onto a germanium plate. Nuclear magnetic resonance spectra were recorded on Bruker DPX250, DPX300 and DPX500 instruments operating at 250, 300 and 500 MHz, respectively. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, q_i = quintet, m = multiplet, dd = doublet of doublets, ddd = double doublet of doublets, ddt = double doublet of triplets, b = broad. Solvents were dried according to established methods, unless purchased dry from Aldrich in sure-seal bottles. The term ether refers to diethyl ether and the term petrol refers to the 40–60 °C boiling point fraction of petroleum ether. All the compounds are named according to the IUPAC system and names were obtained using the ACD/*i*-Lab software version 4.5.

Experimental for compounds **19**–**22** and **23**–**26** have been reported earlier [25,18].

4.1. General procedure for Sonagashira coupling-deprotection [9]

The iodoaniline (20.0 mmol) and trimethylsilylacetylene (4.58 ml, 32.4 mmol) were added to DMF (120 ml). To this solution was added triethylamine (6 ml, 43.1 mmol), copper(I) iodide (760 mg, 4 mmol) and tetraakis(triphenylphosphane)palladium(0) (480 mg, 0.45 mmol) and the solution stirred at r.t. for 16 h. Water (100 ml) was added to the mixture and the aqueous phase extracted with ether (2 × 100 ml). The combined organic phase was washed with water (4 × 60 ml), dried ($MgSO_4$) and evaporated to dryness. The residue was then passed through a column of silica eluting with 1:1 v/v diethyl ether–pentane or pure ether. The product fractions were combined and evaporated to dryness and the residual pale brown oil was dissolved in THF (170 ml), the solution cooled to 0 °C, tetrabutylammonium fluoride (48.38 ml, 1.0 M in THF, 48.4 mmol) added and the mixture stirred at r.t. for 16 h [10]. The solution was then diluted with ether (150 ml), washed with sat. aq. ammonium chloride (160 ml), water (200 ml), brine (160 ml), dried ($MgSO_4$), filtered and the filtrate evaporated to dryness. The residue was chromatographed eluting with EtOAc–pentane mixtures to afford the product (overall yields reported), generally as a clear, pale yellow oil.

4.1.1. N-benzyl-2-ethynylaniline (**3a**)

The product (3.07 g, 82%) was obtained as a colourless oil. (Found: C, 86.65; H, 6.50; N, 6.75. $C_{15}H_{13}N$ requires: C, 86.95; H, 6.30; N, 6.75%); ν_{max}/cm^{-1} 1601, 1575, 1508, 1452, 1324 and 1282; δ_H (250 MHz), 7.59 (dd, $J = 7.6$, 1.7 Hz, 1H, ArH), 7.36–7.16 (m, 7H, ArH), 6.79 (dd, $J = 7.7$, 1.2Hz, 1H, ArH), 5.40 and 4.39 (AB, 2× d, $J = 14.3$ Hz, 2× 1H, NCH_2Ph) and 3.32 (s, 1H, C–H); *m*/*z* (%) 207(M^+, 80), 130(53) 91(100) and 65(24).

4.1.2. N-(2-ethynylbenzyl)aniline (**3b**)

The product (3.07 g, 82%) was obtained as a pale yellow gum. (Found: C, 86.70; H, 6.35; N, 6.85. $C_{15}H_{13}N$ requires: C, 86.95; H, 6.30; N, 6.75%); ν_{max}/cm^{-1} 1696, 1684, 1653, 1498, 1369, 1353 and 1264; δ_H (250 MHz), 7.52 (dd, $J = 7.5$, 1.3 Hz, 1H, ArH), 7.41 (dd, $J = 7.6$ Hz, 0.6 Hz, 1H, ArH), 7.31 (td, $J = 7.4$, 1.4 Hz, 1H, ArH), 7.25–7.22 (m, 1H, ArH), 7.17 (t, $J = 7.5$ Hz, 2H, ArH), 6.71 (t, $J = 7.3$ Hz, 1H, ArH), 6.63 (dd, $J = 7.7$, 0.8 Hz, 2H, ArH), 4.51 (d, $J = 5.7$ Hz, 2H, NCH_2Ar) and 4.22 (bs, 1H, NH); *m*/*z* (%) 207(M^+, 100).

4.2. General procedure for carbamyl chloride formation [11]

The amine (7.21 mmol) was dissolved in DCM (92 ml) and sat. aq. sodium bicarbonate (92 ml) added. The resulting biphasic solution was then cooled to 0 °C and phosgene (1.93 M in toluene, 9.0 ml, 17.37 mmol) added dropwise over 5 min to the rapidly stirred solution. The mixture was left stirring for 10 min, the organic phase separated and the aqueous layer washed with DCM (2 × 50 ml). The combined organic phase was dried ($MgSO_4$), filtered and the filtrate evaporated to dryness. The residue was chromatographed eluting with ether–pentane mixtures or used without further purification.

4.2.1. 2-Ethynylbenzyl(phenyl)carbamyl chloride (**4b**)

The product (0.95 g, 49%) was obtained as a pale pink oil. (Found: C, 71.10; H, 4.55; N, 5.2. $C_{16}H_{12}NClO$ requires: C, 71.25; H, 4.45; N, 5.2%); ν_{max}/cm^{-1} 1732, 1494, 1376, 1228, 1198 and 965; δ_H (250 MHz), 7.45–7.22 (m, 7H, ArH), 7.07–7.06 (m, 2H, ArH), 5.13 (s, 2H, NCH_2Ph) and 3.11 (s, 1H, CH); *m*/*z* (%) 270 (M^+ $^{35}Cl + H$, 66), 234(48), 207(36) and 115(100).

4.2.2. Benzyl(2-ethynylphenyl)carbamyl chloride (**4a**)

The product (3.51 g, 93%) was isolated as colourless prisms from diethyl ether–hexane, m.p. 34–36 °C. (Found:

C, 71.15; H, 4.60; N, 5.15. $C_{16}ClH_{12}NO$ requires: C, 71.25; H, 4.45; N, 5.20%); ν_{max}/cm^{-1} 1734, 1487, 1376, 1201, 1199 and 849; δ_H (250 MHz), 7.59 (dd, $J = 7.6$, 1.7 Hz, 1H, ArH), 7.36–7.16 (m, 7H, ArH), 6.79 (dd, $J = 7.7$, 1.2 Hz, 1H, ArH), 5.40 and 4.39 (AB, 2× d, $J = 14.3$ Hz, 2× 1H, NCH_2Ph) and 3.32 (s, 1H, CH); *m/z* (%) 269 (M^{+} ^{35}Cl, 4), 233(24), 204(13), 143(65) and 91(100).

4.2.3. Benzyl(3-butynyl)carbamyl chloride (5)

The product (1.06 g, 96%) was obtained as a colourless oil. (Found: C, 64.85; H, 5.50; N, 6.25. $C_{12}H_{12}NClO$ requires: C, 65.00; H, 5.40; N, 6.30%); ν_{max}/cm^{-1} 1728, 1456, 1400, 1185, 1156 and 1032; δ_H (250 MHz, 1:1 mixture of rotamers), 7.41–7.19 (m, 5H, ArH), 4.85 and 4.70 (s, 2H, NCH_2Ph), 3.58 and 3.50 (t, $J = 7.1$ Hz, 2H, NCH_2), 2.51 (td, $J = 7.1$, 2.7 Hz, 2H, NCH_2CH_2) and 2.07 and 2.04 (t, $J = 2.7$ Hz, 1H, CH); *m/z* (%) 222 ($M + H^{+}$ ^{35}Cl, 71), 186(7), 129(8) and 91(100).

4.2.4. Benzyl(2-isopropenyl)carbamyl chloride (7)

The product (1.85 g, 76%) was obtained as a colourless oil. (Found: C, 71.30; H, 5.80; N, 4.85. $C_{17}ClH_{16}NO$ requires: C, 71.45; H, 5.60; N, 4.90%); ν_{max}/cm^{-1} 1734, 1489, 1375, 1222, 1195 and 908; δ_H (250 MHz), 7.33–7.05 (m, 7H, ArH), 7.03–6.99 (dd, $J = 5.1$, 3.6 Hz, 1H, ArH), 6.71 (dd, $J = 7.9$, 1.6 Hz, 1H, ArH), 5.40 and 4.09 (AB, 2× d, $J = 14.3$ Hz, 2× 1H, NCH_2Ph), 5.32 (qu., $J = 1.5$ Hz, 1H, $=CH_2$), 5.14 (q, $J = 0.8$ Hz, 1H, $=CH_2$) and 2.16 (q, $J = 0.9$ Hz, 3H, CH_3); *m/z* (%) 250($M - Cl$, 29) and 229(9).

4.3. General procedure for cyclisation–anion capture

The carbamyl chloride (1.0 mmol), palladium(II) acetate (22.4 mg, 10 mol%), trisubstituted phosphane (20 mol%) and tributylstannane (1.1 mmol) were added to toluene or THF (15–20 ml) and the mixture heated to at 23–90 °C for 0.1–30 h. The solution was then evaporated to dryness, the residue dissolved in diethyl ether (50 ml) and 10% aq. potassium fluoride (50 ml) solution added. The biphasic mixture was rapidly stirred at r.t. for 16 h, the diethyl ether layer separated and evaporated to dryness. The residue was chromatographed eluting with EtOAc–pentane or diethyl ether–pentane mixtures to afford the product.

4.3.1. (3Z)-1-benzyl-3-(3-phenyl-2-propynylidene)-1,3-dihydro-2H-indol-2-one (8)

The product (271 mg, 81%) was obtained as pale orange prisms from diethyl ether–pentane, m.p. 127–128 °C. (Found: C, 85.90; H, 5.20; N, 3.90. $C_{24}H_{17}NO$ requires: C, 85.95; H, 5.05; N, 4.20%); ν_{max}/cm^{-1} 1705, 1611, 1469, 1357, 1172 and 1103; δ_H (250 MHz), 7.67 (m, $J = 2.3$ Hz, 2H, ArH), 7.48 (d, $J = 7.4$ Hz, 1H, ArH), 7.39–7.17 (m, 9H, ArH), 6.99 (m, 1H, ArH), 6.87 (s, 1H, =CH), 6.69 (d, $J = 7.8$ Hz, 1H, ArH) and 4.99 (s, 2H, NCH_2Ph); *m/z* (%) 335(M^{+}, 100), 258(39) and 91(89).

4.3.2. (3Z)-1-benzyl-3-(2-thienylmethylene)-1,3-dihydro-2H-indol-2-one (9)

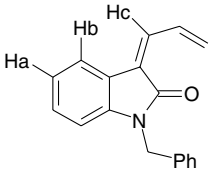
The product (279 mg, 88%) was obtained as pale orange rods from EtOAc–hexane, m.p. 128–129 °C. (Found: C, 74.80; H, 4.80; N, 4.25. $C_{20}H_{15}NOS \cdot 0.25H_2O$ requires: C, 74.65; H, 4.80; N, 4.35%); ν_{max}/cm^{-1} 1686, 1615, 1469, 1343, 1170 and 1104; δ_H (250 MHz), 7.85 (d, $J = 3.4$ Hz, 1H, thienyl H), 7.79 (s, 1H, =CH), 7.66 (d, $J = 5.1$ Hz, 1H, thienyl H), 7.54 (d, $J = 7.4$ Hz, 1H, ArH), 7.36–7.14 (m, 7H, ArH), 7.04 (t, $J = 7.5$ Hz, 1H, ArH), 6.74 (d, $J = 7.7$ Hz, 1H, ArH) and 5.04 (s, 2H, NCH_2Ph); *m/z* (%) 317(M^{+}, 100).

4.3.3. (3Z)-1-benzyl-3-(2-propenylidene)-1,3-dihydro-2H-indol-2-one (10)

The product (112 mg, 43% from carbamyl chloride; 39 mg, 15% from aryl iodide) was obtained as an orange gum. (Found (HRMS): 545.2210 ($2M + Na^{+}$). $C_{18}H_{15}NO$ requires: 545.2205); ν_{max}/cm^{-1} 1701, 1607, 1466, 1354, 1179 and 934; δ_H (250 MHz), 7.63 (d, $J = 7.5$ Hz, 1H, ArH), 7.40 (d, $J = 12.1$ Hz, 1H, $=CH_c$), 7.35–7.24 (m, 6H, Ar*H*/C*H*=CH_2), 7.16 (td, $J = 7.7$, 1.3 Hz, 1H, ArH), 7.01 (td, $J = 7.7$, 1.0 Hz, 1H, ArH_a), 6.71 (d, $J = 7.8$ Hz, 1H, ArH_b), 5.92 (dd, $J = 15.5$, 1.0 Hz, 1H, $=CH_2$), 5.81 (dd, $J = 10.7$, 1.6 Hz, 1H, $=CH_2$) and 4.97 (s, 2H, NCH_2Ph); *m/z* (%) 262($M + H^{+}$, 29), 91(100), 81(17), 69(30) and 55(44).

nOe data:

irradiated H	enhancement / %	
	a	c
b	7.9	7.7

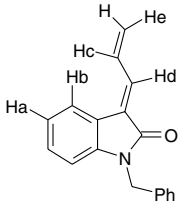


4.3.4. (3E)-1-benzyl-3-(2-propenylidene)-1,3-dihydro-2H-indol-2-one (11)

The product (85 mg, 33% from carbamyl chloride; 143 mg, 55% from aryl iodide) was obtained as an orange gum. (Found (HRMS): 284.1057($M + Na^{+}$). $C_{18}H_{15}NO$ requires: 284.1051); ν_{max}/cm^{-1} 1695, 1610, 1469, 1347, 1169 and 1008; δ_H (250 MHz), 8.15 (dt, $J = 17.0$, 11.4 Hz, 1H, CH_c=CH_2), 7.43 (d, $J = 7.1$ Hz, 1H, ArH), 7.32–7.11 (m, 6H, ArH), 7.17 (d, $J = 11.4$ Hz, 1H, $=CH_d$), 6.98 (td, $J = 7.6$, 1.0 Hz, 1H, ArH_a), 6.68 (d, $J = 7.8$ Hz, 1H, ArH_b), 5.80–5.68 (m, 2H, $=CH_2$) and 4.94 (s, 2H, NCH_2Ph); *m/z* (%) 262($M + H^{+}$, 29), 249(8), 232(5), 183(5) and 91(100).

nOe data:

irradiated H	enhancement / %		
	a	c	e
b	9.7	18.9	-
d	-	-	6.1



4.3.5. (4Z)-2-phenyl-4-(2-thienylmethylene)-1,4-dihydro-3(2H)-isoquinolinone (**12**)

The product (250 mg, 87%) was obtained as pale yellow prisms from diethyl ether–pentane, m.p. 180–182 °C. (Found: C, 75.60; H, 4.95; N, 4.30. $C_{20}H_{15}NOS$ requires: C, 75.70; H, 4.75; N, 4.40%); ν_{max}/cm^{-1} 1653, 1595, 1408, 1286, 1216 and 1203; δ_H (250 MHz), 7.64 (d, $J = 7.4$ Hz, 1H, ArH), 7.49–7.24 (m, 10H, ArH/=CH), 7.19 (dd, $J = 7.3$, 0.5 Hz, 1H, ArH), 7.06 (dd, $J = 5.1$, 3.7 Hz, 1H, furyl H) and 4.86 (s, 2H, NCH_2Ar); *m/z* (%) 318($M + H^+$, 100), 288(26) and 207(17).

4.3.6. (3Z)-1-benzyl-3-(2-furylmethylene)-2-pyrrolidinone (**13**)

The product (76 mg, 60%) was obtained as colourless prisms from diethyl ether–hexane, m.p. 62–63 °C. (Found: C, 75.85; H, 5.95; N, 5.50. $C_{16}H_{15}NO_2$ requires: C, 75.90; H, 5.95; N, 5.55%); ν_{max}/cm^{-1} 1678, 1442, 1421, 1272, 1084 and 1008; δ_H (250 MHz), 7.87 (d, $J = 3.5$ Hz, 1H, furyl H), 7.40 (d, $J = 1.1$ Hz, 1H, furyl H), 7.38–7.26 (m, 5H, ArH), 6.61 (t, $J = 2.3$ Hz, 1H, =CH), 6.50–6.47 (m, 1H, ArH), 4.55 (s, 2H, NCH_2Ph), 3.33 (t, $J = 6.9$ Hz, 2H, NCH_2) and 2.85 (td, $J = 7.0$, 2.3 Hz, 2H, NCH_2CH_2); *m/z* (%) 254($M + H^+$, 100), 91(43) and 69(21).

4.3.7. 1-Benzyl-3-methyl-3-(2-thienylmethyl)-1,3-dihydro-2H-indol-2-one (**14**)

The product (279 mg, 84%) was obtained as colourless prisms from diethyl ether, m.p. 118–119 °C. (Found: C, 75.45; H, 5.70; N, 4.05. $C_{21}H_{19}NOS$ requires: C, 75.65; H, 5.70; N, 4.20%); ν_{max}/cm^{-1} 1709, 1612, 1489, 1467, 1455 and 1359; δ_H (250 MHz), 7.29 (dd, $J = 6.9$, 1.2Hz, 1H, ArH), 7.18–7.14 (m, 5H, ArH), 7.10 (td, $J = 7.0$, 1.5 Hz, 1H, ArH), 6.96 (dd, $J = 5.1$, 1.1 Hz, 1H, thienyl H), 6.79–6.76 (m, 1H, ArH), 6.73–6.70 (m, 1H, ArH), 6.63 (d, $J = 3.3$ Hz, 1H, thienyl H), 6.49 (dd, $J = 6.9$, 1.4 Hz, 1H, ArH), 5.06 and 4.50 (AB, 2× d, $J = 15.9$ Hz, 2× 1H, NCH_2Ph), 3.53 and 3.30 (AB, 2× d, $J = 14.2$ Hz, 2× 1H, CH_2) and 1.55 (s, 3H, CH_3); *m/z* (%) 334($M + H^+$, 100), 252(25) and 236(77).

4.3.8. 1,2-Dibenzyl-3-methyl-1,3-dihydro-2H-indol-2-one (**15**)

The product (79 mg, 47%) was obtained as a pale yellow oil. δ_H (250 MHz), 7.28–7.03 (m, 9H, ArH), 6.89 (dd, $J = 6.9$, 1.5 Hz, 2H, ArH), 6.63 (dd, $J = 7.8$, 2.3 Hz, 2H, ArH), 6.42–6.38 (m, 1H, ArH), 5.02 and 4.45 (AB, 2× d, $J = 16.0$ Hz, 2× 1H, NCH_2Ph), 3.25 and 3.13 (AB, 2× d, $J = 13.0$ Hz, 2× 1H, $PhCH_2$) and 1.55 (s, 3H, CH_3); *m/z* (%) 328($M + H^+$, 100), 252(20), 236(33) and 91(70).

4.4. General procedure for cyclisation–anion capture with in situ generated tributylstannyl-1,2-dialkylidenecyclopentanes

Tris(dibenzylideneacetone)dipalladium (26.3 mg, 2.5 mol%) was added to a stirred solution of the 1,6-diyne (1.15 mmol) in dry THF (11.5 ml) at room temperature under an atmosphere of nitrogen, followed by dropwise addition of Bu_3SnH (0.396 ml, 1.50 mmol) via a syringe pump over 90 min. The resulting solution was stirred for a further 1 h before being concentrated in vacuo to give the dienylstannane as a dark brown oil which was dissolved in dry toluene (15 ml) and aryl iodide (1.15 mmol) and tris(2-furyl)phosphane (26.7 mg, 10 mol%) added. The resulting mixture was stirred and heated at 80–100 °C (oil bath temperature) for 16–17 h then cooled to room temperature and concentrated in vacuo. The residue was dissolved in ether (10 ml) and stirred at room temperature for 2 h with 20% aqueous potassium fluoride (5 ml). The organic layer was separated, dried ($MgSO_4$), filtered and the filtrate concentrated. The residue purified by flash chromatography.

4.4.1. Dimethyl(3Z)-3-[2-(3-methyl-2,3-dihydro-1-benzofuran-3-yl)ethylidene]-4-methylene-1,1-cyclopentanedicarboxylate (**28**)

Prepared from diyne (**19**) (239 mg, 1.15 mmol) and aryl iodide (**23**) (315 mg, 1.15 mmol) by the general procedure over 16 h at 90 °C. The crude product was subjected to flash chromatography eluting with 1:4 v/v ether/petroleum ether to afford the product (276 mg, 67%) which crystallised from ether–petroleum ether as colourless needles, m.p. 115–118 °C. (Found C, 70.80; H, 6.95. $C_{21}H_{24}O_5$ requires: C, 70.75; H, 6.80%); δ (250 MHz), 1.37 (s, 3H, Me), 2.50–2.71 (m, 2H, $=CHCH_2$), 2.96 and 3.02 (2× s, 2× 2H, $C(CH_{22})$), 3.71 and 3.72 (2× s, 2× 3H, 2× OMe), 4.15 and 4.34 (2× d, 2× 1H, $J = 9.0$ Hz, OCH_2), 5.13 and 5.17 (2× s, 2× 1H, $=CH_2$), 5.41 (t, 1H, $J = 7.0$ Hz, $=CHCH_2$), 6.77 (d, 1H, $J = 8.0$ Hz, ArH), 6.85 (t, 1H, $J = 6.0$ Hz, ArH) and 7.06–7.15 (m, 2H, ArH); *m/z* (%) 356(M^+, 22), 281(25), 224(77), 178(30), 133(100) and 105(59).

4.4.2. Dimethyl(4Z)-3-methylene-4-{2-[3-methyl-1-(phenylsulfonyl)-2,3-dihydro-1H-indol-3-yl]ethylidene}-1,1-cyclopentanedicarboxylate (**29**)

Prepared from diyne (**19**) (239 mg, 1.15 mmol) and aryl iodide (**24**) (474 mg, 1.15 mmol) by the general procedure over 17 h at 100 °C. Work up followed by flash chromatography eluting with 3:2 v/v ether/petroleum ether afforded the product (366 mg, 64%) which crystallised from ether/petroleum ether as colourless prisms, m.p. 112–114 °C. (Found C, 65.20; H, 5.95; N, 2.65. $C_{27}H_{29}NO_6S$ requires: C, 65.45; H, 5.90; N, 2.85%); δ (250 MHz), 1.12 (s, 3H, Me), 2.31 and 2.42 (2× dd, 2× 1H, $J = 7.0$, 16.0 Hz, $=CHCH_2$), 2.86 and 3.01 (2× s, 2× 2H, $C(CH_2)_2$), 3.57 and 3.78 (2× d, 2× 1H, $J = 10.0$ Hz, NCH_2), 3.72 and 3.73 (2× s, 2× 3H, 2× OCH_3), 5.02 and 5.08 (2× s, 2× 1H, $=CH_2$), 5.18 (t, 1H, $J = 7$ Hz, $=CHCH_2$), 6.95–7.05 (m, 2H, ArH), 7.21 (m, 1H, ArH), 7.41–7.56 (m, 3H, ArH), 7.66 (d, 1H, $J = 8.0$ Hz) and 7.81 (m, 2H, ArH). *m/z* (%) 495(M^+, 14), 420(18), 354(6), 272(100), 163(9), 130(58) and 77(74).

*4.4.3. Dimethyl(3Z)-3-[2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)ethylidene]-4-methylene-1,1-cyclopentanedicarboxylate (**30**)*

Prepared from diyne (**19**) (248 mg, 1.15 mmol) and aryl iodide (**25**) (346 mg, 1.15 mmol) by the general procedure over 17 h at 100 °C. Work up followed by flash chromatography eluting with 3:2 v/v ether/petroleum ether afforded the product (305 mg, 70%) which crystallised from ether/petroleum ether as colourless prisms, m.p. 107–109 °C. (Found: C, 68.65; H, 6.80; N, 3.35. $C_{22}H_{25}NO_5$ requires: C, 68.90; H, 6.55; N, 3.65%); δ (250 MHz), 1.39 (s, 3H, Me), 2.66–2.88 (m, 6H, =CHCH_2, C$(CH_2)_2$), 3.23 (s, 3H, NMe), 3.65 and 3.70 (2× s, 2× 3H, 2× OMe), 5.11–5.16 (m, 3H, =CH_2, =CHCH_2), 6.86 (d, 1H, $J = 8.0$ Hz, ArH), 7.01 (t, 1H, $J = 7.0$ Hz, ArH) and 7.16–7.21 (m, 2H, ArH); *m/z* (%) 383(M^+, 32), 352(28), 276(18), 223(49), 161(100) and 103(18).

*4.4.4. (2Z)-8,8-dimethyl-2-[2-(3-methyl-2,3-dihydro-1-benzofuran-3-yl)ethylidene]-3-methylenespiro[4.5]decane-6,10 dione (**31**)*

Prepared from diyne (**20**) (248 mg, 1.15 mmol) and aryl iodide (**23**) (315 mg, 1.15 mmol) by the general procedure over 16 h at 90 °C. Work up followed by flash chromatography eluting with 3:7 v/v ether/petroleum ether afforded the product (296 mg, 70%) which crystallised from ether/petroleum ether as colourless needles, m.p. 125–127 °C. (Found: C, 79.05; H, 7.70. $C_{24}H_{28}O_3$ requires: C, 79.10; H, 7.75%); δ (250 MHz) 0.96 and 1.01 (2× s, 2× 3H, Me_2C), 1.37 (s, 3H, Me), 2.52–2.65 (m, 6H, =CHCH_2, Me_2C(C$H_2)_2$), 2.82 and 2.91 (2× s, 2× 2H, C$(CH_2)_2$), 4.15 and 4.35 (2× d, 2× 1H, $J = 7$ Hz, OCH_2), 5.11 and 5.15 (2× s, 2 × 1H, =CH_2), 5.35 (t, 1H, $J = 7.0$ Hz, =CHCH_2), 6.79 (d, 1H, $J = 8.0$ Hz, ArH), 6.87 (t, 1H, $J = 7.0$ Hz, ArH) and 7.06–7.16 (m, 2H, ArH); *m/z* (%) 364(M^+, 14), 280(6), 232(6), 133(100), 105(34) and 77(7).

*4.4.5. (3Z)-8,8-dimethyl-2-methylene-3-{2-[3-methyl-1-(phenylsulfonyl)-2,3-dihydro-1H-indol-3-yl]ethylidene}-spiro[4.5]decane-6,10-dione (**32**)*

Prepared from diyne (**20**) (248 mg, 1.15 mmol) and aryl iodide (**24**) (346 mg, 1.15 mmol) by the general procedure over 17 h at 100 °C. Work up followed by flash chromatography eluting with 7:3 v/v ether/petroleum ether afforded the product (390 mg, 62%) which crystallised from ether/petroleum ether as colourless prisms, m.p. 104–106 °C. (Found: C, 71.65; H, 6.70; N, 2.85. $C_{30}H_{33}NO_4S$ requires: C, 71.55; H, 6.60; N, 2.80%); δ (250 MHz) 0.97 and 1.01 (2× s, 2× 3H, Me_2C), 1.12 (s, 3H, Me), 2.32 and 2.50 (2× dd, 2× 1H, $J = 7.0$, 16.0 Hz, =CHCH_2), 2.58–2.65 (m, 4H, Me_2C(C$H_2)_2$), 2.73 and 2.88 (2× s, 2× 2H, C$(CH_2)_2$), 3.56 and 3.78 (2× d, 2× 1H, $J = 10.0$ Hz, NCH_2), 5.00 and 5.06 (2× s, 2× 1H, =CH_2), 5.15 (t, 1H, $J = 7.0$ Hz, =CHCH_2), 6.96–7.03 (m, 2H, ArH), 7.21 (m, 1H, ArH), 7.40–7.58 (m, 3H, ArH), 7.65 (d, 1H, $J = 8.0$ Hz, ArH) and 7.80–7.85 (m, 2H, ArH); *m/z* (%) (FAB) 504($M^+ + 1$, 15), 272(100), 132(18) and 83(7); ν_{max}(film) 2956, 1727, 1695, 1168, 1093 and 957 cm^{-1}.

*4.4.6. (2Z)-2[2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)ethylidene]-8,8-dimethyl-3-methylenespiro[4.5]decane-6,10-dione (**33**)*

Prepared from diyne (**20**) (248 mg, 1.15 mmol) and aryl iodide (**25**) (346 mg, 1.15 mmol) by the general procedure over 17 h at 100 °C. Work up followed by flash chromatography eluting with 7:3 v/v ether/petroleum ether to afford the product (364 mg, 72%) which crystallised from ether/petroleum ether as colourless prisms, m.p. 111–113 °C (Found: C, 76.65; H, 7.65; N, 3.30. $C_{25}H_{29}NO_3$ requires: C, 76.70; H, 7.45; N, 3.60%); δ (250 MHz) 0.96 and 0.97 (2× s, 2× 3H, Me_2C), 1.38 (s, 3H, Me), 2.54 and 2.56 (2× s, 2× 3H, Me_2C(C$H_2)_2$), 2.65–2.89 (m, 6H, =CHCH_2, C$(CH_2)_2$), 3.22 (s, 3H, NMe), 5.09–5.19 (m, 3H, =CH_2, =CHCH_2), 6.85 (d, 1H, $J = 8.0$ Hz, ArH), 7.07 (t, 1H, $J = 8.0$ Hz, ArH) and 7.19 and 7.32 (m, 2H, ArH); *m/z* (%) 391(M^+, 80), 373(9), 307(17), 250(22), 213(27), 161(100), 129(19) and 55(8).

*4.4.7. (2Z)-8,8-dimethyl-2-[2-(4-methyl-3,4-dihydro-1H-isochromen-4yl)ethylidene]-3-methylenespiro[4.5]decane-6,10-dione (**34**)*

Prepared from diyne (**20**) (248 mg, 1.15 mmol) and aryl iodide (**26**) (331 mg, 1.15 mmol) by the general procedure over 17 h at 90 °C. Work up followed by flash chromatography eluting with 2:3 v/v ether/petroleum ether afforded the product (281 mg, 62%) which crystallised from ether/petroleum ether as colourless needles, m.p. 117–119 °C (Found C, 79.10; H, 8.10. $C_{25}H_{30}O_3$ requires: C, 79.35; H, 8.00%); δ (250 MHz) 0.96 and 1.00 (2× s, 2× 3H, Me_2C), 1.27 (s, 3H, Me), 2.52–2.73 (m, 6H, =CHCH_2, Me_2C(C$H_2)_2$), 2.81 and 2.90 (2× s, 2× 2H, C$(CH_2)_2$), 3.35 and 3.75 (2× d, 2× 1H, $J = 11$ Hz, OCH_2), 4.78 (s, 2H, OCH_2Ar), 5.11 and 5.23 (2× s, 2× 1H, =CH_2), 5.37 (t, 1H, $J = 7.0$ Hz, =CHCH_2), 6.95 (m, 1H, ArH) and 7.13–7.30 (m, 4H, ArH); *m/z* (%) 378(M^+, 19), 361(11), 247(5), 147(18), 57(74) and 43(100).

*4.4.8. 3-Methyl-3-[(2E)-2-(4-methylenedihydro-3(2H)-furanylidene)ethyl]-2,3-dihydro-1-benzofuran (**35**)*

Prepared from diyne (**21**) (108 mg, 1.15 mmol) and aryl iodide (**23**) (315 mg, 1.15 mmol) by the general procedure over 16 h at 90 °C. Work up followed by flash chromatography eluting with 1:4 v/v ether/petroleum ether afforded the product (184 mg, 62%) as a colourless oil. (Found: C, 78.95, H, 7.10. $C_{16}H_{18}O_2$ requires: C, 79.30; H, 7.50%); δ (250 MHz), 1.42 (s, 3H, Me), 2.59–2.71 (m, 2H, =CHCH_2), 4.19 and 4.39 (2× d, 2H, $J = 9.0$ Hz, OCH_2), 4.38 and 4.44 (2× s, 2× 2H, O$(CH_2)_2$), 5.11 and 5.28 (2× s, 2× 1H, =CH_2), 5.46 (t, 1H, $J = 7.0$ Hz, =CHCH_2), 6.81 (d, 1H, $J = 8.0$ Hz, ArH), 6.89 (t, 1H, $J = 7.0$ Hz, ArH) and 7.08–7.16 (m, 2H, ArH); *m/z* (%) 242(M^+, 18), 233(63), 205(12), 165(18), 133(100), 105(51) and 77(10); ν_{max}(film) 2958, 1733, 1596, 1480, 1229, 976 and 831 cm^{-1}.

4.4.9. (3E)-1-benzyl-3-[2-(3-methyl-2,3-dihydro-1-benzofuran-3-yl)ethylidene]-4-methylenepyrrolidine (**36**)

Prepared from diyne (**22**) (210 mg, 1.15 mmol) and aryl iodide (**23**) (315 mg, 1.15 mmol) by the general procedure over 16 h at 100 °C. Work up followed by flash chromatography eluting with 1:1 v/v ether/petroleum ether afforded the product (257 mg, 62%) as a viscous colourless oil. (Found C, 83.00; H, 7.15; N, 3.85. $C_{23}H_{25}NO$ requires: C, 83.35; H, 7.60; N, 4.25%); δ (250 MHz), 1.36 (s, 1H, Me), 2.58–2.66 (m, 2H, =CHCH_2), 3.22 and 3.30 (2× s, 2× 2H, N$(CH_2)_2$), 3.59 (s, 2H, NCH_2Ph), 4.16 and 4.39 (2× d, 2× 1H, $J = 8.0$ Hz, OCH_2), 5.09 and 5.20 (2× s, 2× 1H, =CH_2), 5.41 (t, 1H, $J = 7.0$ Hz, =C*H*CH_2), 6.79 (d, 1H, $J = 8.0$ Hz, ArH), 6.88 (t, 1H, $J = 7.0$ Hz, ArH) and 7.20–7.31 (m, 5H, ArH); *m*/*z* (%) 331(M^+, 14), 316(6), 198(37), 133(92), 91(100) and 65(13).

4.4.10. 4-Methyl-4-[(2E)-2-(4-methylenedihydro-3(2H)-furanylidene)ethyl]-3,4-dihydro-1H-isochromene (**37**)

Prepared from diyne (**21**) (108 mg, 1.15 mmol) and aryl iodide (**26**) (331 mg, 1.15 mmol) by the general procedure over 16 h at 90 °C. Work up followed by flash chromatography eluting with 1:4 v/v ether/petroleum ether afforded the product (183 mg, 62%) as a viscous yellow oil. (Found: C, 79.25; H, 7.7. $C_{17}H_{20}O_2$ requires: C, 79.65, H, 7.85%); δ (250 MHz), 1.30 (s, 3H, Me), 2.62 and 2.82 (2× dd, 1H, $J = 7.0$, 16.0 Hz), 3.58 and 3.80 (2× d, 2H, $J = 11.0$ Hz, OCH_2), 4.37 and 4.44 (2× s, 2× 2H, O$(CH_2)_2$), 4.81 (s, 2H, OCH_2Ar), 5.11 and 5.38 (2× s, 2× 1H, =CH_2), 5.48 (t, 1H, $J = 7.0$ Hz, =C*H*CH_2), 6.98 (d, 1H, $J = 8.0$ Hz, ArH) and 7.14–7.31 (m, 3H, ArH); *m*/*z* (%) 256(M^+, 10), 225(14), 197(18), 178(27), 165(67), 147(100), 119(90), 77(13) and 43(26); ν_{max}(film) 2953, 1727, 1489, 1386 and 1097 cm^{-1}.

4.4.11. (3E)-1-benzyl-3-[2-(4-methyl-3,4-dihydro-1H-isochromen-4-yl)ethylidene]-4-methylenepyrrolidine (**38**)

Prepared from diyne (**22**) (210 mg, 1.15 mmol) and aryl iodide (**26**) (331 mg, 1.15 mmol) by the general procedure over 17 h at 90 °C. Work up followed by flash chromatography eluting with 1:1 v/v ether/petroleum ether afforded the product (277 mg, 70%) as a viscous colourless oil. (Found: C, 83.30; H, 7.90; N, 4.20. $C_{24}H_{27}NO$ requires: C, 83.45; H, 7.90; N, 4.05%); δ (250 MHz), 1.29 (s, 3H, Me), 2.56 and 2.78 (2× dd, 2× 1H, $J = 7.0$, 16.0 Hz, =CHCH_2), 3.19 and 3.31 (2× s, 2× 2H, N$(CH_2)_2$), 3.56 and 3.76 (2× d, 2× 1H, $J = 11.0$ Hz, OCH_2), 3.59 (s, 2H, NCH_2Ph), 4.78 (s, 2H, OCH_2Ar), 5.09 and 5.30 (2× s, 2× 1H, =CH_2), 5.41 (t, 1H, $J = 7.0$ Hz, =C*H*CH_2), 6.95 (m, 1H, ArH) and 7.11–7.32 (m, 8H, ArH); *m*/*z* (%) 345(M^+, 13), 330(6), 254(7), 198(77), 147(27), 119(37), 91(100) and 65(13); ν_{max}(film) 2956, 1733, 1700, 1456, 1289 and 1026 cm^{-1}.

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