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# Palladium Catalysed Tandem Cyclisation-Anion Capture Processes. Part 1. Background and Hydride Ion Capture by Alkyl- and π-Allyl-Palladium Species[1].

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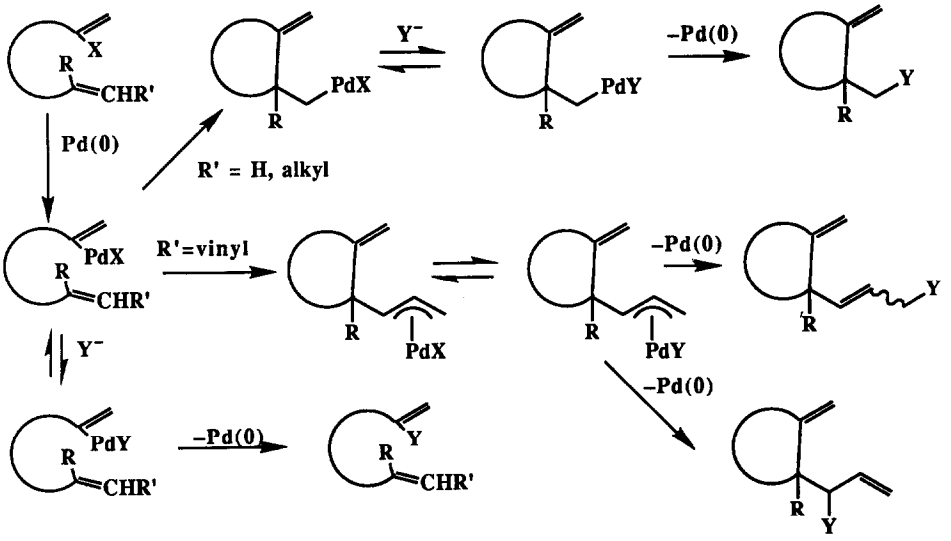
*Key Words:* Palladium, catalysis, cyclisation, hydride capture, tandem process.

*Abstract: A new, wide ranging, synthetically powerful, catalytic tandem cyclisation-anion capture process is proposed which depends on the rate of cyclisation of an organopalladium specifies (RPdX) onto a proximate alkene or diene being significantly faster than anion exchange and reductive elimination in the sequence RPdX → RPdY → RY + Pd(0). The catalytic cyclisation - anion capture sequence is illustrated for hydride capture by a wide variety of substrates giving rise to fused- and spiro-, carbo- and hetero-cyclic systems, regio- and stereo-specifically.*

Palladium salts and complexes are exceptionally versatile catalysts for the construction of carbon-carbon and carbon-heteroatom bonds[2]. Much recent attention has focused on the Heck reaction[3] due to developments which have considerably enhanced the scope of this palladium-catalysed vinylation of aryl, heteroaryl, vinyl and benzyl halides. Thus the Heck reaction has been extended to the synthesis of bridged rings, spirocycles, and tetrasubstituted carbon centres.[4-6] These latter developments and the ongoing high level of activity have been further foster by the advent of a range of additives which variously enhance the rate of Heck reactions, the regioselectivity of the β-hydride elimination step, and which suppress double bond isomerisation in the product. Thus addition of tetraalkylammonium chlorides or hydrogen sulphates often allow Heck reactions to be carried out at, or near, room temperature in good yield,[7] whilst addition of Ag(1) salts[8] or Tl(1)[9] salts can control the direction of β-hydride elimination, suppress double bond isomerisation and influence the reaction rate. Tl(1) additives have also proved useful in natural product synthesis.[10]

Our earlier observations on various palladium catalysed cyclisation processes clearly showed the kinetic preference for a 5-exo-trig cyclisation mode as compared to a 6-endo-trig cyclisation.[4,11] The success of the intramolecular Heck reaction depends on the availability of a suitably located hydrogen atom for a β-hydride elimination. Absence of such a β-hydrogen usually precludes catalytic cyclisation although sometimes a cyclisation-rearrangement intervenes.[12] If the initial alkyl-, vinyl- or π-allyl-palladium species arising from a

palladium catalysed cyclisation onto a proximate alkene, alkyne, or 1,3-diene moiety respectively, lacks a β-hydride elimination pathway we believed it might be possible to intercept the organopalladium(11) intermediate via an "anion" exchange process. Scheme 1 illustrates this concept for cyclisations of aryl- or vinyl- palladium species onto proximate alkenes and 1,3-dienes. Cyclisations onto proximate alkynes generating vinylpalladium species will be dealt with in a subsequent paper. Note that the initial or starter Pd(11) species can conceptually be generated from alkyl-, allyl-, aryl- or vinyl-X species although for brevity the first two species are not shown in the scheme.



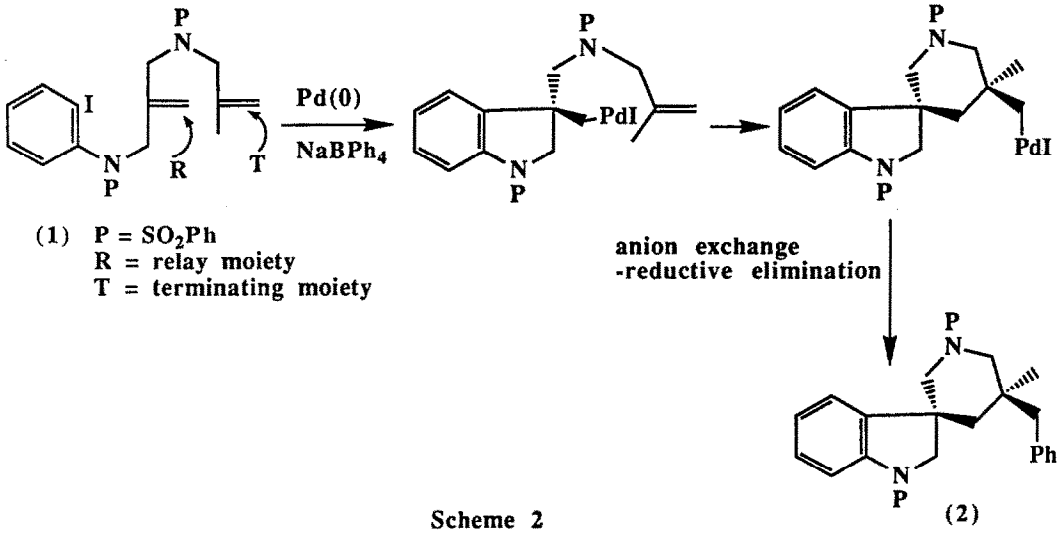

**Scheme 1**

Insertion of Pd(0) into a suitable C-X bond (X=Br,I,OTf etc) generates the organopalladium (11) species which can cyclise onto a proximate alkene or 1,3-diene moiety to generate alkyl- and π-allyl-palladium (11) species respectively. Exchange of X for a new "anion" Y can then occur. If the new "anion" Y facilitates a reductive elimination the catalytic cycle becomes established resulting in a new ring forming process which is accompanied by the introduction of functionality Y in a regio- and stereo- defined way. Incorporation of the blocking substituent R on the proximate alkene is necessary to prevent β- hydride elimination although incorporation of R into the dienyl substrates is likely to be unnecessary since β- hydride elimination from palladium π-allyl species is known to be slow.[13] An alternative strategy to a blocking group R (Scheme 1) is to utilise bridgehead strain effects (Bredt's rule)[14] and several examples of this will be described below. The use of the word "anion" in the context of Scheme 1 is meant to embrace both ionic and covalent sources of Y and is felt to be more appropriate that the term cross-coupling. The efficiency of Scheme 1 will depend on a fast cyclisation step compared to anion exchange and reductive elimination. In the absence of this rate advantage direct coupling of Y without cyclisation will be a competitive process (Scheme 1) and in unfavourable cases may occur to the exclusion of the desired cyclisation-anion capture process. Our experience to date indicates that when the cyclisation step involves formation of 3-6 membered rings the direct capture process does not effectively compete with cyclisation-anion capture.

The full potential of the cyclisation-anion capture concept remains to be explored but the scope of the process is emphasised by Table 1 which incorporates the, as yet little explored, polycyclisation-anion capture strategy.

**Table 1** Potential Combinations for (Poly) Cyclisation Anion-Capture Processes.

| Starter Species | Relay Species (R) | Terminating Species (T) | Y |
|---|---|---|---|
| alkyl | alkene | alkene | anionic [H,OAc CN, $SO_2Ph$,$CH(CO_2R)_2$] |
| aryl | alkyne | alkyne | neutral (amines, MeOH/CO,acrylates) |
| vinyl | 1,2-diene | 1,2-diene | organometallics RM[M=Sn(1V), |
| allyl | 1,3-diene | 1,3-diene | B(111),Zn(11] |




(1) P = $SO_2Ph$
R = relay moiety
T = terminating moiety

Scheme 2

Any starter moiety can conceptually be combined with any relay moiety, any terminating moiety, and any anion transfer reagent. Moreover, the relay phase can, in principle, incorporate several successive cyclisations before engaging the terminating moiety. The "anion" transfer reagents listed in the Table are illustrative rather than exhaustive and much further development remains to be done in this area. It should be noted that when the terminating species is a 1,3-diene the resulting π-allylpalladium (11) species can undergo the anion capture step in two mechanistically distinct ways depending on the nature of Y. Thus Y can attack as an external nucleophile [Y = $CH(CO_2R)_2$, CN, OAc, amines] in which case the nucleophile attacks trans to the Pd(11), or Y can be transferred to the π-allyl moiety via the Pd(11) ion i.e. cis with respect to Pd(11) (Y = H, alkyl, aryl, CO). The regio- and stereo- chemical outcome is thus dependant on the nature of Y.[16] A typical examples of processes encompassed by Table 1 is shown (Scheme 2) by the cyclisation of (1) to a single diesteromer of (2).[15] Here we have an aryl starter species combined with a single alkene relay (R) and alkene terminator (T) (1, R and T) followed by anion ($Ph^-$) transfer from sodium tetraphenylborate. The process occurs in anisole at 100°C in 63% yield.

We have achieved examples of monocyclisation processes which employ all the starter, terminating and anion

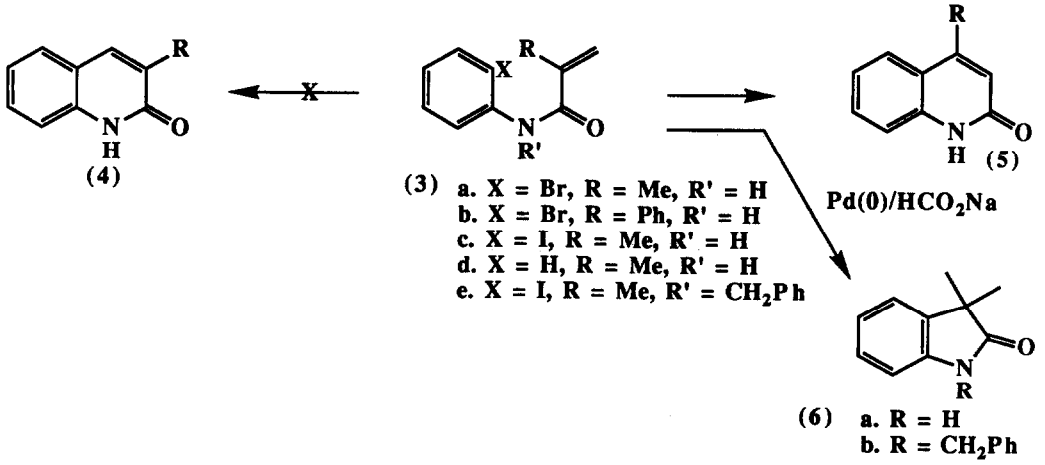
capture species listed in Table 1[1,17-19] together with several biscyclisation anion capture processes employing aryl iodide starter species and alkene or alkyne relay and terminating species.[20] Additionally we have employed biscyclisation processes to create strained polyfused ring systems incorporating cyclopropyl and cyclobutyl rings. Recently others have reported monocyclisation processes employing CO[22] and acrylates[23] as the "anion" capture moiety.

In this paper we report full details of our work in which the terminating species is an alkene or 1,3-diene and the anion capture agent is hydride ion. A range of potential hydride ion sources was surveyed: formic acid-piperidine, metal formates, $NaBH_4$, $LiAlH_4$, $Ph_2SiH_2$, $Bu_3SnH$ and i-PrOH. Formic acid-piperidine and metal formates (usually sodium formate) proved the most effective. Four catalyst systems have been employed for the majority of reactions described in this paper.

**CATALYST A:** 10mol % $Pd(OAc)_2$, 20mol % $PPh_3$, sodium formate (1.1mol), tetraethylammonium chloride (1mol), DMF as solvent.
**CATALYST B:** Identical to A but with acetonitrile as solvent.
**CATALYST C:** 10mol % $Pd(OAc)_2$, 20mol % $PPh_3$, piperidine (4mol), formic acid (3mol), DMF as solvent.
**CATALYST D:** 5mol% $Pd(OAC)_2$, 10mol% $PPh_3$, sodium formate(1mol), DMF as solvent.
No detailed study of catalyst optimisation has been carried.

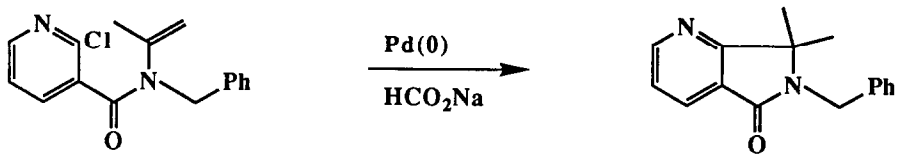
**Aryl Halide Starter Species with Alkene Terminating Species**

**(i) Monocyclisation Forming Fused Rings.** Heck and Terpko[12] attempted to achieve a palladium catalysed 6-endo-trig cyclisation of (3a) and (3b) to the corresponding quinolones (4) since the alternative catalytic 5-exo-trig process is precluded by lack of a β-hydride elimination pathway. In the event the products, which were obtained in 43 and 36% yield respectively, were the rearranged quinolones (5a) and (5b).

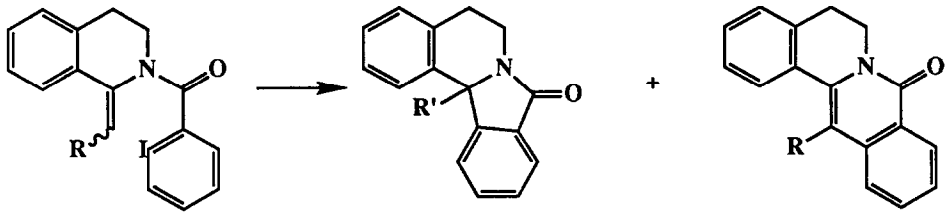



We initially studied the cyclisation of (3c) in the presence of palladium acetate and tri o-tolylphosphine (MeCN, 60°C) over 24h. The reaction was slow [56% of (3c) remained unreacted] and gave a mixture of direct capture product (3d)(27%) and cyclisation-anion capture product (6)(16%). Thus the direct capture rate was more favourable than the cyclisation-anion capture rate. However, when the reaction was repeated in boiling acetonitrile in the presence of tetraethylammonium chloride (1mol) the sole product was (6a)(68%). In no case

did we detect any quinolone products (4) or (5). An analogous cyclisation of (3e) with catalyst system B afforded (6b)(80%) as the sole product, whilst (7), with catalyst system A, afforded (8)(54%).




(7) (8)



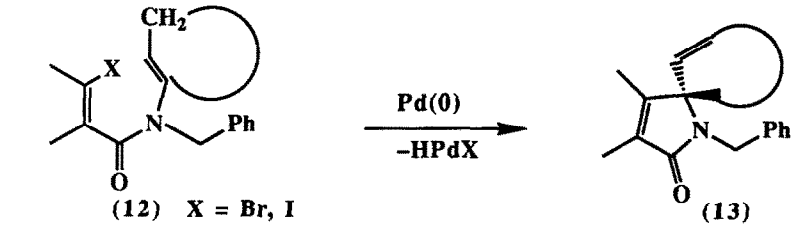

(9) a. R = H
b. R = Me

(10) a. R' = Me
b. R' = $CH{=}CH_2$

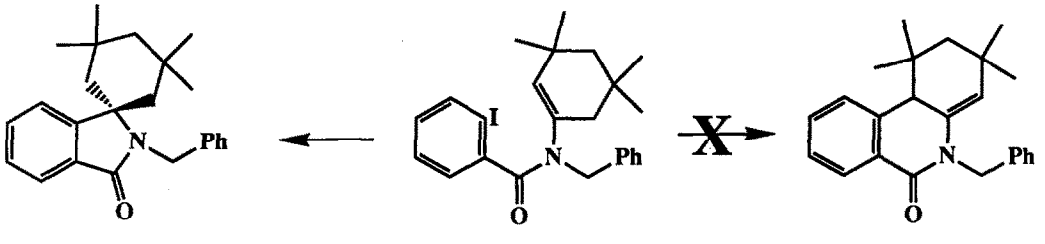
(11) a. R = H
b. R = Me

We have previously shown the enamide (9a)[24] undergoes palladium catalysed 6-endo-trig cyclisation to afford (11a) in 57% yield, whilst (9b) gives a 14:1 mixture of (10b) and (11b) under the most selective catalytic conditions.[4] The hydride capture methodology offers the potential for generating a tetasubstituted carbon centre at a ring junction. Hence we studied the cyclisation of (9a) in DMF at 80°C using catalyst system A. The reaction furnished a 2:1 mixture of (10a) and (11a). Thus under these conditions the 5-exo-trig cyclisation-hydride capture competes with a 6-endo-trig cyclisation-β-hydride elimination sequence. Attempts were made to improve the selectivity for (10a) by carrying out the cyclisation in the presence of Tl(1) salts, and by varying the phosphine (tri-o-tolyl and tri-2-furyl) but in all these cases the 6-endo-trig cyclisation product (11a) predominated.

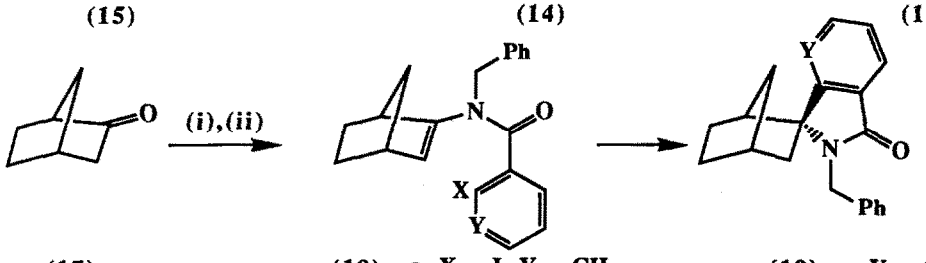
**(ii) Monocyclisation Forming Spirocyclic rings.** We have previously shown that enamides derived from a wide range of cyclic ketones undergo regiospecific 5-exo-trig cyclisation-β-hydride elimination (12)→(13) to produce spirocyclic compounds in good yield. It was therefore of interest to study the cyclisation of (14) in which the kinetically favoured 5-exo-trig cyclisation-hydride capture is in competition with a 6-endo-trig-β-hydride elimination sequence. Cyclisation (80°C) of (14) using catalyst system D afforded spirocycle (15)(50%). None of the alternative 6-endo-trig cyclisation (16) was observed.



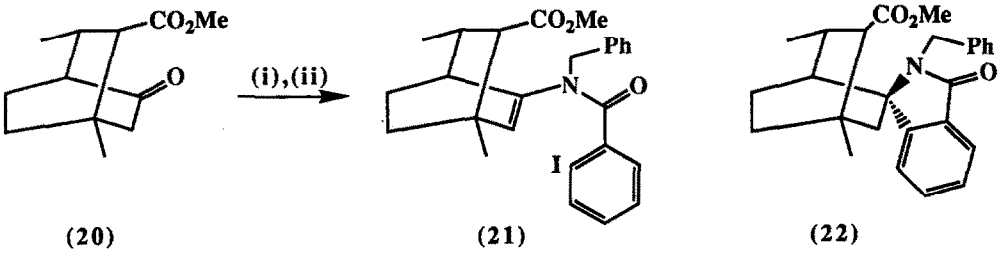

(12) X = Br, I (13)




(15) (14) (16)




(17) (18) a. X = I, Y = CH
b. X = Cl, Y = N
(19) a. Y = CH
b. Y = N

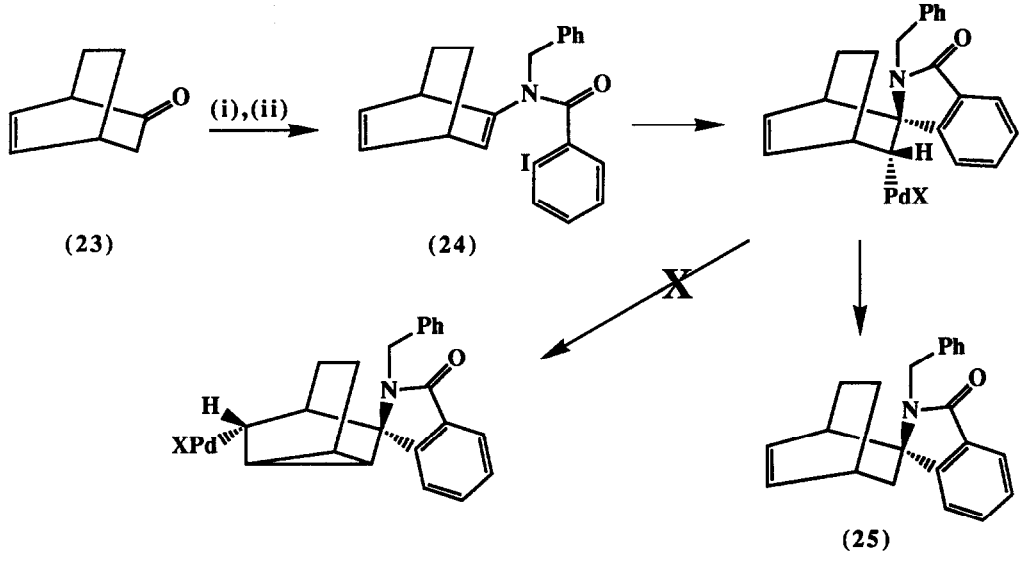



(20) (21) (22)

**(i) $PhCH_2NH_2$/benzene (ii) 2-iodobenzoyl chloride/$Et_3N$/benzene**

Cyclisation-hydride capture was studied in a series of bicyclic enamides in which β-hydride elimination was precluded by bridgehead strain effects (Bredt's rule). Thus the ketones (17) and (20) were converted to the enamides (18) and (21) by conventional methodology. Enamides (18a) and (18b) were cyclised regio- and stereo- specifically to the spirocycles (19a) and (19b), in 65 and 60% yield respectively, using catalyst system A. The stereochemistry of the spirocycles was established by n.O.e. studies. In particular a positive n.O.e. effect was observed between the syn-proton of the methylene bridge of (19) and the aryl ring protons. Ketone (20) was prepared from 3-methyl-2-cyclohexenone and methyl crotonate via a double Michael addition.[25] The

enamide (21) derived from (20) was cyclised (DMF, 110°C) regio- and stereo- specifically in 55% yield by catalyst system B. The stereochemistry of (22) was also established by n.O.e. studies. Thus irradiation of the signal at δ 3.73 ($CO_2Me$) effected an enhancement (9.2%) of the benzylic methylene protons at δ 5.32. No n.O.e. enhancements were observed in the aromatic proton region of the spectrum.




(i) $PhCH_2NH_2$/benzene (ii) 2-iodobenzoyl chloride/benzene/$Et_3N$

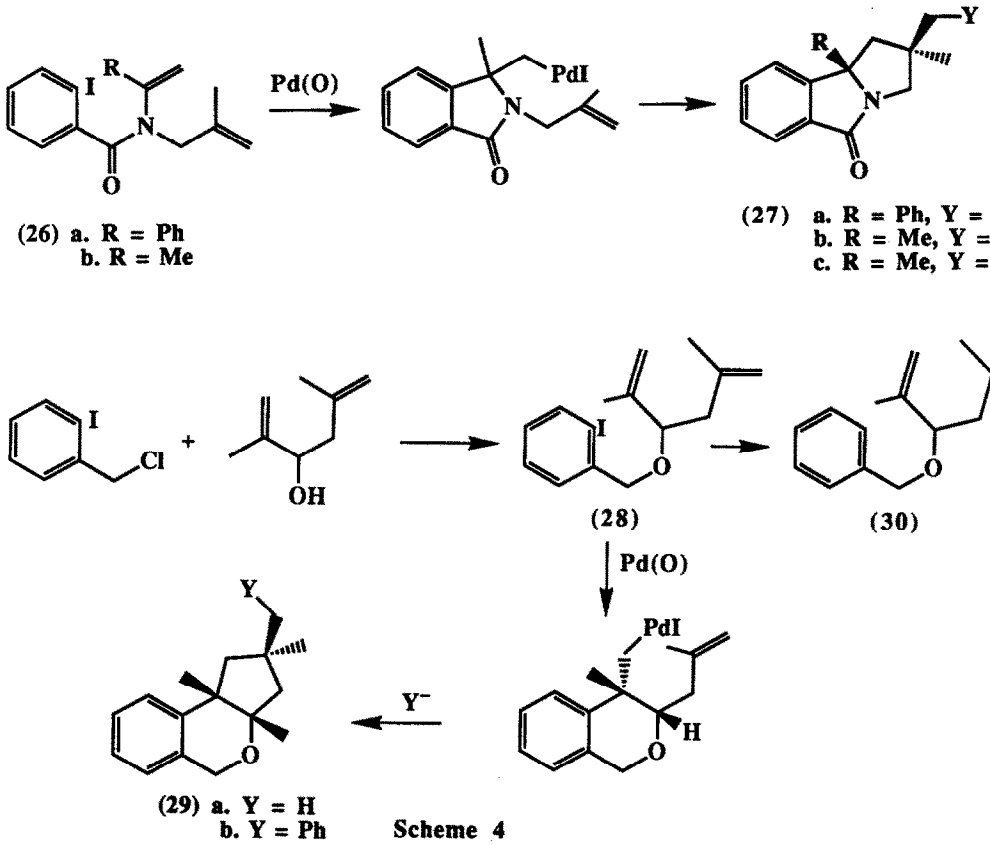
**Scheme 3**

Ketone (23)[26] was converted into enamide (24) by conventional methodology (Scheme 3). Cyclisation (DMF, 110°C) of enamide (24) using catalyst system C occurred regio- and stereo-specifically to give spirocycle (25). The expected alkylpalladium (11) intermediate (Scheme 3) has the potential for a further cyclisation by engaging the remaining double bond (Scheme 3). Cyclisations similar to this have recently been reported by us[21]. However, no cyclopropyl containing products were detected in this case. The stereochemistry of (25) is based on n.O.e. data. In particular irradiation of the $N\underline{CH_2}Ph$ signal at δ 4.9 caused enhancement of the two nearest bridging methylene protons $H_A$(4.5%) and $H_B$(2.7%). In all the cases involving bridged ring enamides the stereochemical outcome of the palladium catalysed cyclisation-hydride capture processes in analogous to that established for both electrophilic addition and pericyclic processes involving the corresponding bicycloalkenes.

**(iii) Biscyclisation Forming Fused and Spirocyclic Rings via an Alkene Relay.** We and others have developed biscyclisation processes which generate fused-, spirocyclic- and bridged- ring products via a β-hydride elimination termination step.[4,27-30] However, the biscyclisation-anion capture process offers a significant advantage over these in that it allows addition of another functional group at the eventual cyclisation terminus. We have reported our preliminary observations on this latter process which displays both regio- and stereo- specificity in the examples so far studied.[20]

Enamides (26a,b) were prepared by acylation of the corresponding ketone imines with 2-iodobenzoyl chloride. These substrates have alkene relay and terminating species and both undergo regiospecific 5-exo-trig

biscyclisation (DMF, 80°C) followed by hydride capture to afford the tricyclic products (27a,b) in 60-70% yield using catalyst system A.




**Scheme 4**

The biscyclisation substrate (28) was synthesised from 2-iodobenzyl chloride and the corresponding secondary alcohol.[31] Cyclisation (MeCN, 80°C, 36h) of (28) by catalyst system B, but without the tetraethylammonium chloride, was slow and incomplete (Table 2). The cyclisation was therefore studied in the presence of a range of additives (Table 2).

**Table 2** Effect of additives on the biscyclisation-hydride capture of (28)[a]

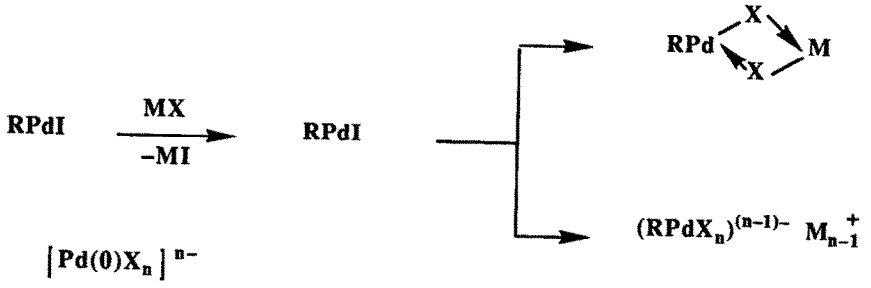
| Additive[b] | Time(h) | Product Ratio | | | Yield(%) |
|---|---|---|---|---|---|
| | | (28) | (29) | (30) | |
| - | 36 | 1 | 4 | - | 65 |
| $Et_4NCl$ | 2 | - | 3 | 2 | 70 |
| $AgNO_3$ | 6 | 1 | 3.5 | - | 68 |
| $TlNO_3$ | 6 | 1 | 4.6 | - | 65 |

a. All reactions were carried out in boiling acetonitrile.

b. 1mol equiv. of additive was used in each case.

c. A minor amount of an unidentified product was detected.

Table 2 indicates that addition of tetraethylammonium chloride promotes the direct capture process (28)→(30) as well as speeding up the rate of reaction. Both silver nitrate and thallium(1) nitrate promote the desired reaction but do not result in any direct capture product. The precise role of Tl(1) and Ag(1) salts in these processes is not yet clear. Initially they will give rise to anion exchange on the intermediate organopalladium (11) species with precipitation of TlI and AgI respectively. The large excess of the additives could then give rise to either anion-bridged binuclear species or anionic Pd(11) and/or Pd(0) complexes (Scheme 5)

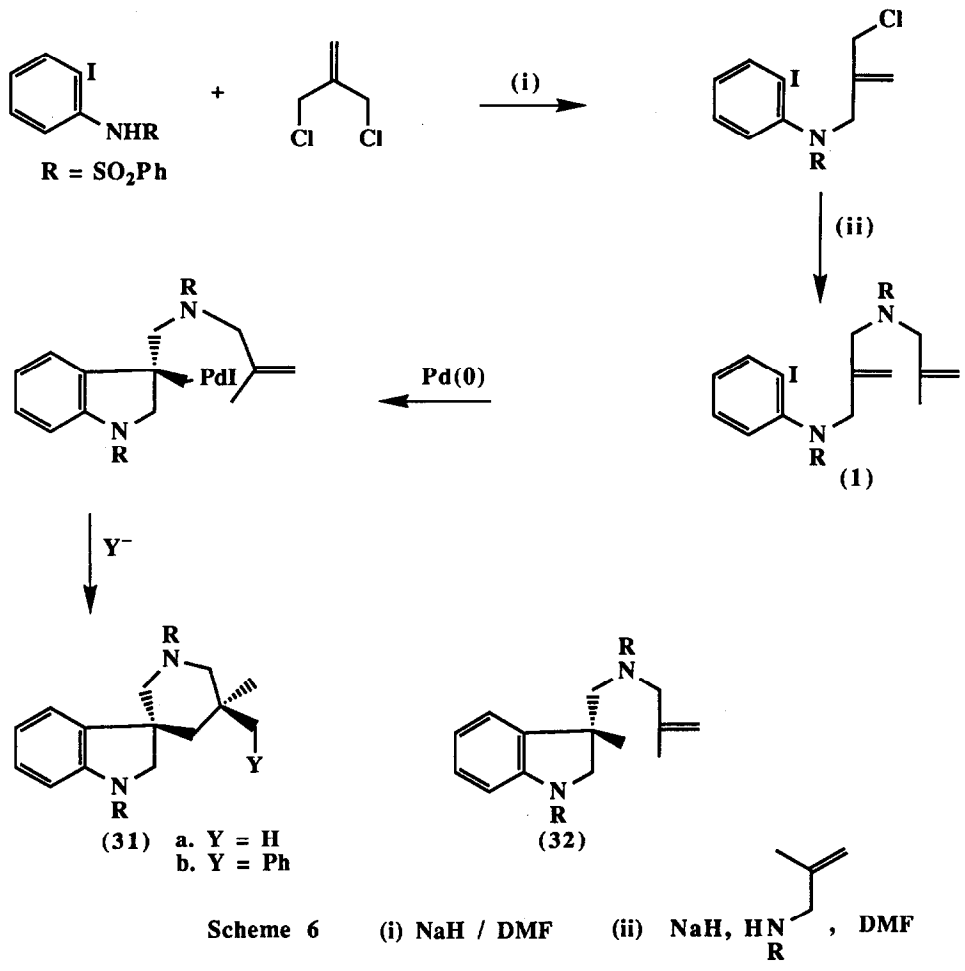


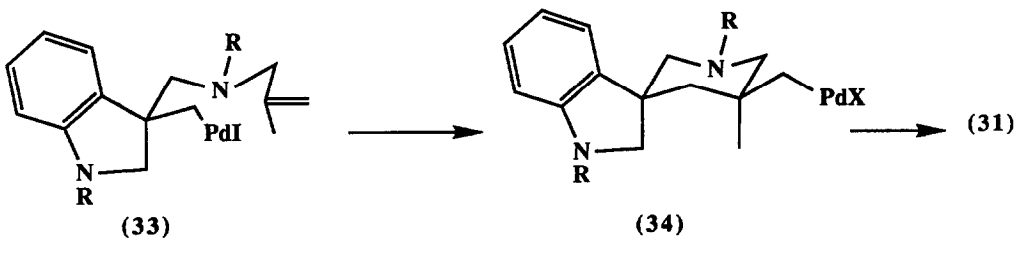

**Scheme 5**

Evidence that polychloro complexes of Pd(0) stabilise and solubilise the zerovalent state has recently been presented.[32] The anion-bridged binuclear species would be expected to be kinetically very labile when X is an oxyanion due to the low oxophilicity of Ag(1) and Tl(1). The results in Table 2 and other studies with Ag(1) and Tl(1) salts[8-10] show there are discernable differences between Ag(1) and Tl(1) salts and thus require the metal ion to have a role in the overall process.

The cyclisation of (26a,b) to (27a,b) and of (28) to (29) occurs both regio- and stereo- specifically and, as studies with sodium tetraphenylborate (Y=Ph) show,[27] the anion transfer occurs to generate the $CH_2Y$ functionality cis to the ring junction Me group, i.e. to give (27c) and (29b).[33] The stereochemistry of (27c) and (29a,b) accords with the cyclisation generating the most stable ring junction stereochemistry with the stereochemistry of the $CH_2Y$ group involving transfer of Y to the least hindered face of the developing tricyclic systems.

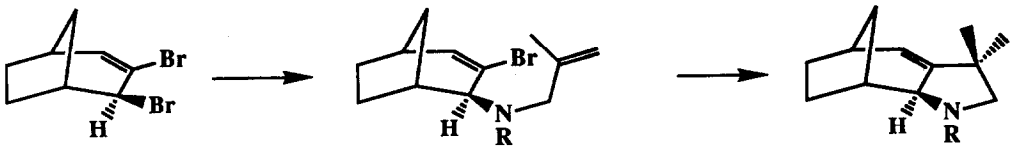
The spirocyclic precursor (30) was synthesised as outlined in Scheme 6. Palladium catalysed cyclisation (DMF, 100°C, 4h, catalyst system D) in the presence of sodium formate (1.2mol) afforded a 2:3 mixture of (31a) and (32) in 50% yield. Thus in this case hydride ion capture was competitive with the second (6-exo-trig) cyclisation. However, the bis-cyclisation anion capture product (31a) became the major product in the presence of $Tl_2CO_3$(2mol). Thus cyclisation (DMF, 80°C, 48h) in the presence of this additive afforded a 4:1 mixture of (31a) and (32). The spirocycle (31b) was obtained as a single diasteromer when sodium tetraphenylborate was used as the anion transfer agent.[27] A chair-like pre-transition state conformer (33) in which the bulky aryl and PdI groups are equatorial and which gives rise to an equatorial $CH_2PdX$ moiety (34) seems energetically most favourable.




**B. Vinyl Halide Starter Species with Alkene Terminating Species.** To date only one example of this combination. The substrate (36) was prepared from the known dibromide (35).

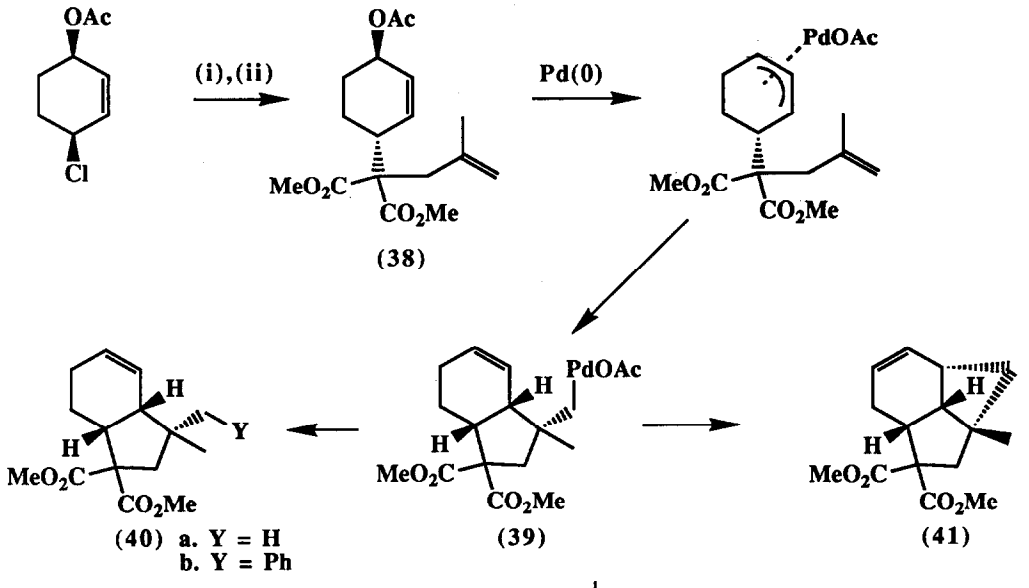
Cyclisation of (36) to (37)(74%) was achieved at 80°C using catalyst system A. Product stereochemistry is based on the appearance of a singlet for $H_A$ at δ3.4 in the p.m.r. spectrum of (37).




(35) (36) R = $SO_2Ph$ (37)

Cyclisation of (36) to (37)(74%) was achieved at 80°C using catalyst system A. Product stereochemistry is based on the appearance of a singlet for $H_A$ at δ3.4 in the p.m.r. spectrum of (37).

**C. Allylic Acetate Starter Species with Alkene Terminating Species.** Only one example, involving monocyclisation, of this combination has been studied thus far. The substrate (38) was prepared as outlined in Scheme 7 utilising chemistry developed by Bäckvall et al.[34]



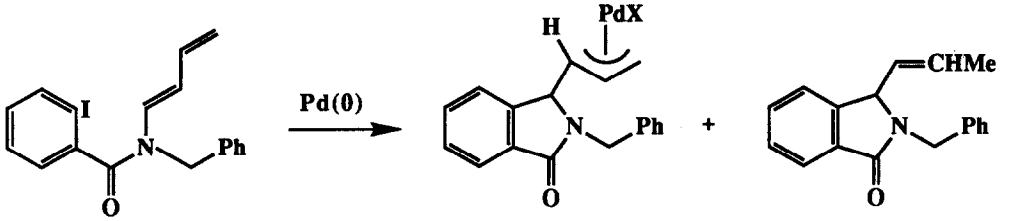

Scheme 7. (i) NaH, 

, DMF

Compound (38) was cyclised in acetonitrile (80°C) using formic acid (5mol) as the hydride source (catalyst system C). The stereochemistry depicted in Scheme 7 is based on the expected intermediate π-allylpalladium(11) species in which the palladium coordinates trans to the leaving group (OAc). Cyclisation (insertion) then leads to the alkylpalladium(11) species (39). This species then furnishes (40a) by hydride capture. Evidence for the stereochemistry comes from its conversion to (38b) using sodium tetraphenylborate as the anion capture reagent (unpublished), and to (41) in the absence of anion transfer reagents.[21] The stereochemistry also accords with a closely related cyclisation-carbonylation (metallo-ene) sequence reported by Oppolzer.[30]

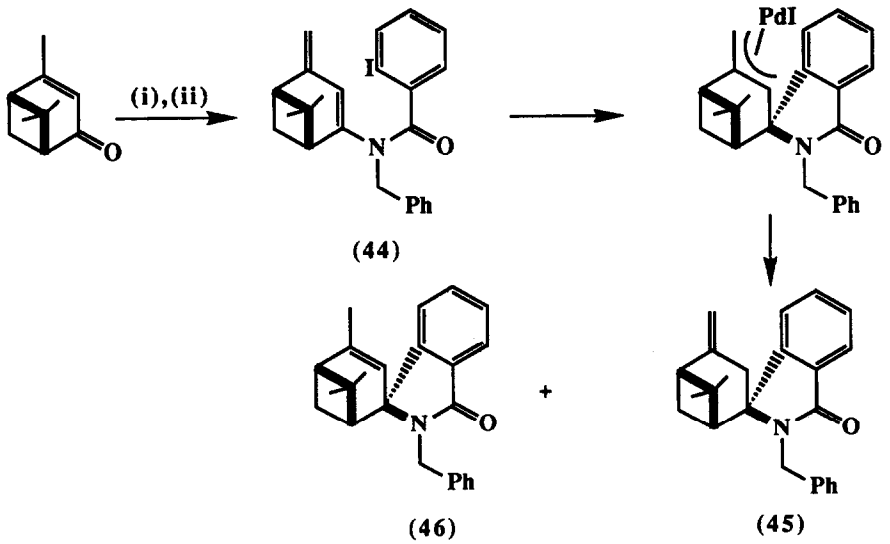
**D. Aryl Halide Starter Species with 1,3-Diene Terminating Species.**

**(i) Monocyclisation Forming Fused Rings.** Substrate (42) was prepared by acylation of the benzylamine imine of crotonaldehyde, and was cyclised in boiling acetonitrile, using catalyst system C, to give (43)(67%) as a 1:2 E/Z-mixture via regiospecific hydride ion transfer.




(42) (43)

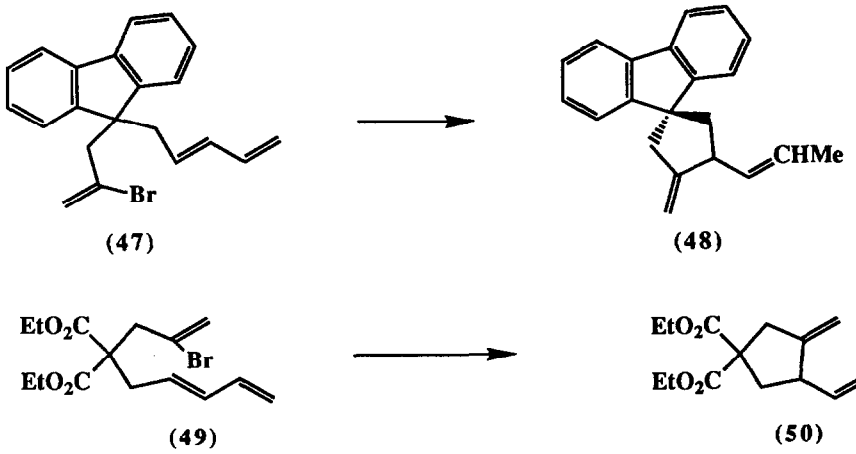
**(ii) Monocyclisation Forming Spirocyclic Rings.** Enamide (44) was prepared from verbenone by standard methodology and cyclised (DMF, 80°C, 24h) regio- and stereo- specifically using catalyst system D to a 4:1 mixture of (45) and (46) (Scheme 8) in 80% combined yield.




**Scheme 8. (i)$PhNH_2$/ benzene (ii) 2-iodobenoyl chloride/ $Et_3N$/ benzene**

The stereochemistry of (45) and (46) accords with the expected 5-exo-trig cyclisation trans to the $CMe_2$ bridge and is based on n.O.e. studies.

**E. Vinyl Halide Starter Species with 1,3-Diene Terminating Species.** The 9,9-disubstituted fluorene (47) was prepared by sequential alkylation of the 9-fluorenyl anion with the corresponding bromides and was cyclised (MeCN,80°C) using catalyst system C. The product (48)(90%), which comprised a 1.3:1 E / Z-mixture of isomers, was derived by regiospecific hydride transfer to the least substituted π-allyl terminus.




(47) (48)

(49) (50)

A similar pattern was observed when the cyclisation-hydride capture protocol was performed on (49) using catalyst system C. The product (50)(77%) comprised a 2:1 E / Z-mixture of isomeric alkenes.

In summary, the tandem cyclisation-anion capture methodology is a powerful new addition to the armoury of carbon-carbon bond forming processes. The regio- and stereo- specificity of the processes allied to the ability to terminate the cyclisation sequence by addition of a wide range of functionality (Table 1, and later papers in this series) allows the maximisation of molecular complexity.

**Experimental.** General experimental details were as previously described.[4]

**Cyclisation substrates.**

**N-Methacryloyl-2-iodoaniline(3c).** 2-Iodoaniline(10.95g, 0.05mol) was added dropwise to a stirred solution of methacrylic anhydride (0.05mol) in pyridine (100ml) [the Brewster method]. The solution was then boiled under reflux for 0.5h, cooled, and left in the refrigerator overnight. 10% Aqueous sodium hydroxide (100ml) was then added and the mixture extracted with ether (2x50ml). The organic layer was dried ($MgSO_4$) and the solvent removed to afford a dark coloured liquid which was distilled to afford the product (4.77g, 33%),b.p. 122°C/0.4mmHg, which solidified to a colourless crystalline mass, m.p. 42-44°C (Found: C,42.0, H, 3.7; N, 5.05. $C_{10}H_{10}INO$ requires C, 41.85; H, 3.5, N, 4.9%); δ 8.35(d, 1H, J 8Hz, ArH), 7.95(br s, 1H,NH), 7.78(d,1H, J 8Hz, ArH), 7.36 and 6.84(2xt, 2x1H, J 8Hz, ArH), 5.97 and 5.53(2xs, 2x1H, = $CH_2$) and 2.12(s, 3H, Me);$\upsilon_{max}$ 3446, 3214, 2926, 1633 and 1581 $cm.^{-1}$; m/z(%) 287($M^+$,30), 246(1), 218(1), 160(100) and 91(14).

**N-Benzyl-N-methacryloyl-2-iodoaniline(3e).** To a stirred solution of N-benzyl-2-iodoaniline (6.85g, 0.22mol) and triethylamine (2.24g), 0.2mol) in dry benzene (50ml) at room temperature was added dropwise methacryloyl chloride (2.9g, 0.28mol) in dry benzene (20ml). The resulting solution was stirred at room temperature for 1.5h, then boiled under reflux for 2h. After cooling, the solvent was removed under reduced pressure and the residue taken up in ether (100ml). The ether was washed with water (2x100ml), dried ($MgSO_4$), and concentrated to afford the product (5.92g, 71%) as a yellow viscous oil which was purified by flash chromatography eluting with 1:1 v/v ether-petroleum ether. HRMS:$M^+$ 377.0272. $C_{17}H_{16}INO$ requires 377.0278. δ 7.86(m, 1H, J 7Hz,

ArH), 7.2(m, 5H, ArH), 7.13 and 6.93(2xt, 2x1H, J 7Hz, ArH), 6.67(d, 1H, J 7Hz, ArH), 5.25 and 5.03(2xs, 2x1H, = $CH_2$), 5.68 and 4.12(2xd, 2x1H, J 14Hz, $NCH_2$) and 1.84(s, 3H, Me); $\upsilon_{max}$ 3082, 2921, 1654, 1575, and 1191 $cm.^{-1}$; m/z(%) 377($M^+$,18), 308(2), 250(30), 203(4), 91(100), 69(44) and 41(36).

**N-Benzyl-N-isopropenyl-2-chloropyridine-3-carboxamide(7).** A solution of the benzylamine imine of acetone (1.47g, 0.01mol) and triethylamine (1.01g, 0.01mol) in dry ether (50ml) was stirred and cooled to 0°C in an ice bath. 2-Chloronicotinyl chloride (1.76g, 0.01mol) in ether (15ml) was added dropwise over 5mins. and the mixture stirred at room temperature for 30 mins., filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography eluting with 1:1v/v ether-petroleum ether. The product (1.31g, 46%) formed colourless needles from ether-petroleum ether, m.p. 82°C. (Found: C, 66.7; H, 5.0; N, 9.35. $C_{16}H_{15}ClN_2O$ requires C, 67.0; H, 5.25; N, 9.75%); δ 8.3 and 7.6(2xdd,2x1H, ArH), 7.4 - 7.2(m, 6H, ArH), 4.8(s, 2H, $NCH_2$), 4.7(d, 2H, C = $CH_2$), and 1.7(s, 3H, Me); m/z(%) 286($M^+$,1), 251(1), 223(20), 132(35), 91(100) and 65(12).

**N-Benzyl-N-(2'-iodobenzoyl)-3,3,5,5-tetramethyl-1-aminocyclohexene(14).** A solution of 2-iodobenzoyl chloride (2.65g, 0.01mol) in dry benzene (20ml) was added dropwise with stirring to a solution of the benzylamine imine of 3,3,5,5-tetramethylcyclohexanone (2.43g, 0.01mol) and triethylamine (1.01g, 0.01mol) in dry benzene (50ml). The resulting mixture was stirred and boiled under reflux for 2h. Work up in the usual way and crystallisation of the residue from ether-petroleum ether afforded the product (2.5g, 55%) as colourless prisms, m.p. 87-89°C. (Found: C,60.75, H, 5.95; N, 2.95. $C_{24}H_{28}INO$ requires C,60.9; H, 5.9; N, 2.95%); δ 7.8-7.0(m, 9H, ArH), 5.2(s, 1H, = CH), 4.8(br s, 2H, $NCH_2$), 1.6(s, 2H, = $CCH_2$), 1.0(s,2H,$CH_2$), and 0.7 and 0.5(2xs, 2x6H, 4xMe); m/z(%) 473($M^+$,44), 458(65), 231(100), 203(24), and 91(30).

**N-Benzyl-N-(2'-iodobenzoyl)-2-aminobicyclo[2.2.1]hept-2-ene(18a).** A solution of 2-iodobenzoyl chloride (5.32g, 0.02mol) in ether (25ml) was added dropwise over 20min. with stirring to an ice cooled solution of bicyclo[2.2.1]hept-2-one benzylamine imine (4.0g, 0.02mol) and triethylamine (2.02g, 0.02mol) in ether (75ml). The mixture was stirred for a further 1h. at room temperature and then filtered. The filtrate was evaporated to dryness to afford the product (8.0g, 93%) which crystallised from ether as colourless prisms, m.p. 87-89°C. (Found: C, 58.4; H, 4.6; N, 3.1; I, 29.5. $C_{21}H_{20}INO$ requires C, 58.7; H, 4.65; N, 3.25; I, 29.55%); δ 7.82(d, 1H, J 8.1 Hz, ArH), 7.4-7.2(m, 7H, ArH), 7.03(dt, 1H, J 8.1 and 2.2Hz, ArH), 5.5(s, 1H), 5.25(br s, 1H), 4.6(d, 1H), 2.6 and 2.3(2xs, 2x1H, $CH_2$), 1.42 and 1.25(2xt, 2x1H) and 0.83-0.42(m,4H,$CH_2CH_2$); m/z(%) 429($M^+$,3), 302(23), 274(56), 231(69), 203(21) and 91(100).

**N-Benzyl-N-(2'-chloropyridin-3-yl)-2-aminobicyclo[2.21]hept-2-ene(18b).** Prepared in an analogous manner to that described above using 2-chloronicotinoyl chloride in place of 2-iodobenzoyl chloride. The reaction mixture was stirred for 5h at room temperature and worked up as above followed by column chromatography eluting with 1:4v/v ether-petroleum ether. The product (72%) crystallised from ether-petroleum ether as colourless needles, m.p. 121-122°C (Found: C, 71.3; H, 5.7; N, 5.7. $C_{20}H_{21}ClNO_2$ requires C, 70.9; H, 5.65; N, 5.25%); δ 8.3 and 7.6(d and dd, 2x1H, ArH), 7.3-7.16(m, 6H,ArH), 5.4(s, 1H, C=CH), 5.0 and 4.65(2xbr s, 2x1H, $NCH_2$), 2.59 and 2.3(2xbr s, 2x1H), 1.4 and 1.3(2xm, 2x1H, $CH_2$), and 0.7 and 0.55(2x br s, 2x2H, $CH_2CH_2$); m/z(%) 338($M^+$,2), 303(5), 275(21), 247(10), 140(20), 112(12) and 91(100).

**Benzylamine imine of methyl 1,3-dimethyl-5-oxobicyclo[2.2.2]octane-2-carboxylate.** Prepared (75%) from

methyl 1,3-dimethyl-5-oxobicyclo[2.2.2]octane-2-carboxylate and benzylamine in boiling benzene (Dean-Stark trap). The product was a pale yellow oil, b.p. 152-154°C/0.1mmHg (Found: C, 76.15; H, 8.35; N, 4.5. $C_{19}H_{25}NO_2$ requires C, 76.2, H, 8.4; N, 4.65%); δ 7.3(m, 5H, ArH), 4.4(s, 2H, $PhCH_2N$), 3.68(s, 3H, OMe), 2.79 (d, 1H, J 18Hz), 2.24(s,2H,$CH_2$), 2.04(d, 1H, J 7.6Hz), 1.92(m, 2H, $CH_2$), 1.7(m, 1H), 1.45(m, 2H, $CH_2$), 1.07 (d,3H,Me) and 0.93(s,3H,Me); m/z(%) 229($M^+$,25), 284(2), 240(3), 208(3), 199(18) and 91(100).

**Methyl N-benzyl-N-(2′-iodobenzoyl)-1,3-dimethyl-5-aminobicyclo[2.2.2]oct-5-ene-2-carboxylate(21).** A solution of 2-iodobenzoyl chloride (8.92g, 0.33mol) in dry benzene (20ml) was added dropwise, with stirring, to a solution of the imine (above) (10g), 0.33mol) and triethylamine (3.38g, 0.33mol) in dry benzene (50ml) at room temperature. The resulting mixture was then stirred and boiled under reflux for 4h, cooled and filtered. The filtrate was evaporated to dryness and the residue crystallised from ether-petroleum ether to afford the product (14.8g, 85%) as colourless prisms, m.p. 68-70°C. (Found: C, 58.55; H, 5.45; N, 2.6. $C_{26}H_{28}$ $INO_3$ requires C, 59.0; H, 5.35; N, 2.65%); δ 7.8(d, 1H, ArH), 7.49(m, 2H, ArH), 7.25(m,5H, ArH), 7.0(m, 1H, ArH), 5.78(br s, 1H, = CH), 5.2-4.7(br s, 2H, $PhCH_2N$), 3.54(s, 3H, OMe), 1.95 and 1.6(2xbr s, 2x1H), 1.3 and 1.1 (2xm, 2x2H), 0.99 and 0.77(s, and br s, 2x3H, 2xMe) and 0.58(m, 1H); m/z(%) 529($M^+$,18), 470(1), 402(6), 302(38), 298(6), 231(100), 91(73) and 76(16).

**N-Benzyl-N-(2′-iodobenzoyl)-2-aminobicyclo [2.2.2] octa-2, 5-diene(24).**

(i) The benzylamine imine of 2-oxobicyclo[2.2.2]oct-5-ene was prepared by reaction with benzylamine in boiling benzene under reflux using a Dean-Stark trap. The product (75%) was a colourless liquid, b.p. 130°C/1.5mm Hg (Found: C,85.15; H,7.45; N,7.4 $C_{15}H_{17}N$ requires C,85.25; H,7.65; N,7.1 %); δ 7.3-7.16(m, 5H,ArH), 6.39-6.27(m, 2H, CH=CH), 4.3(s, 2H, $NCH_2$), 3.28 and 2.89(2xm, 2x1H), 2.10(br s, 2H, $CH_2CO$), and 1.84-1.39(m, 4H, 2x$CH_2$); m/z(%) 211($M^+$,12), 119(9), 91(100), and 79(17); $\upsilon_{max}$(film) 3022 , 2987, 1660, 1498, 740 and 700$cm^{-1}$.

(ii) A solution of 2-iodobenzoylbenzoyl chloride (6.17g, 0.27mol) in dry benzene (20ml) was added dropwise with stirring to a solution of imine (above) (5.74g, 0.27mol) and triethylamine (2.73g, 0.27mol) in dry benzene at room temperature. The resulting mixture was then stirred and boiled under reflux for 2h. After cooling the mixture was filtered, the filtrate evaporated, and the residue crystallised from ether to afford the product (10.38g, 87%) as colourless prisms, m.p. 97-98°C (Found: C, 59.85; H, 4.35; N, 3.1. $C_{22}H_{20}NIO$ requires C, 59.85; H, 4.55; N, 3.15); δ 7.80(m, 1H, ArH), 7.4-7.12(m, 8H, ArH), 5.87(m, 2H, CH=CH), 5.59(m, 1H,=CH), 4.58(d, 2H, $NCH_2$), 3.35 and 3.3(2xm, 2x1H), and 2.12-1.25(m, 4H, 2x$CH_2$); m/z(%) 414($M^+$,17),314(13), 285(53), 231(94) and 91(100); $\upsilon_{max}$(KBr) 3050, 2870, 1650 and 1395$cm.^{-1}$

**N-(2′-Iodobenzoyl)-N-methallyl-1-phenylvinylamine(26a).**

(i) Reaction of methyallylamine with acetophenone in dry methylene chloride in the presence of 4Å molecular sieves over 12h followed by the usual work-up afforded the methallyl imine of acetophenone (60%) as a colourless oil, b.p. 56-60°C/0.02mmHg (Found: C, 83.35; H, 8.9; N, 8.3. $C_{12}H_{15}N$ requires C, 83.2; H, 8.75; N, 8.1%); δ 7.83(m, 2H, ArH), 7.37(m, 3H, ArH), 4.94 and 4.87(2xs, 2x1H,=$CH_2$), 4.06(s, 2H, $CH_2$), and 2.22 and 1.87 (2xs, 2x3H, 2xMe); m/z(%) 173 ($M^+$,82), 172(100), 158(59), 135(15), 118(2) and 104(13).

(ii) A solution of 2-iodobenzoyl chloride (9.24g, 34.7mmol) in dry benzene (20ml) was added dropwise with stirring to a solution of the imine (above) (6.0g, 34.7mmol) and triethylamine (3.5g,34.7mmol) in dry benzene (80ml) under a nitrogen atmosphere. The resulting mixture was stirred at room temperature for a further 4.5h. Work-up in the usual way followed by crystallisation from ether-petroleum ether afforded the product

(9.78g,70%) as pale yellow prisms, m.p. 83-84°C (Found: C, 56.35, H, 4.45; N, 3.25. $C_{19}H_{18}INO$ requires C, 56.6; H, 4.5; N, 3.45%); δ 7.76(d, 1H, ArH), 7.35(s, 5H, ArH), 7.14(m, 2H, ArH), 6.92(m, 1H,ArH), 5.30, 5.21, 4.88 and 4.78(4xs, 4x1H, 2x = $CH_2$), 4.29(br s, 2H, $NCH_2$) and 1.9(s,3H, Me); m/z(%) 403($M^+$,4), 348(2), 276(6), 231(100), 203(22) and 72(11); $\upsilon_{max}$(KBr) 3088, 3025, 2992, 1695, 1622 and 767cm$^{-1}$.

**N-(2′-Iodobenzoyl)-N-methallyl-2-aminopropene(26b).**

(i) The methallylamine imine of acetone was prepared (60%) in analogous manner to that described above. The product was a colourless oil, b.p. 40-42°C/0.1mmHg (Found: C, 75.85; H, 11.55; N, 12.4. $C_7H_{13}N$ requires C, 75.6; H, 11.8; N, 12.6%); δ 4.8(s, 2H,=$CH_2$), 3.8(s, 2H, $NCH_2$), and 2.1, 1.8 and 1.78(3xs, 3x3H, 3xMe); m/z(%) 112($M^+$+l, 84), 111(17), 96(39) and 55(100).

(ii) Prepared (60%) in an analogous manner to that described above. The product was a thick pale yellow oil (Found: C,49.55; H,4.55; N,4.2. $C_{14}H_{16}ION$ requires C,49.3; H,4.75; N,4.1%); δ 7.8-7.0(m, 4H, ArH), 5.0(br s, 2H,=$CH_2$), 4.9 and 4.8(2xs, 2x1H,=$CH_2$), 4.3(br s, 2H, $NCH_2$), and 1.9 and 1.8(2xs, 2x3H, 2xMe); m/z(%) 341($M^+$,7), 231(100), 214(26), 203(22), 186(43) and 96(62).

**O-(2′-Iodobenzoyl)-2,5-dimethylhexa-1,5-diene-3-ol(28).** 2,5-Dimethylhexa-1,5-diene-3-ol(1.26g, 0.01mol) was dissolved in dry DMF(50ml) and sodium hydride (0.5g, 50% w/w in mineral oil) added portionwise with stirring. The mixture was stirred for a further 1h and then a solution of 2-iodobenzoyl chloride (2.52g, 0.01mol) in dry DMF(10ml) was added dropwise over 15min. The resulting mixture was stirred overnight at room temperature, the solvent removed under reduced pressure and the residue partitioned between ether (75ml) and water (50ml). The aqueous layer was separated, extracted with ether (75ml) and the combined ether extracts dried ($Na_2SO_4$) and evaporated. The residual oil was distilled to afford the product (2.5g, 79%) as a colourless oil, b.p. 110°C/0.1mmHg (Found: C, 52.75; H, 5.8. $C_{15}H_{19}IO$ requires C, 52.65; H, 5.55%); δ 7.8-7.0(m, 4H, ArH), 5.0(s, 2H,=$CH_2$), 4.9 and 4.7(2xs, 2H,=$CH_2$), 4.4 and 4.2(2xd, 2H, $OCH_2$), 4.0(t, 1H, =CCHO), 2.5 and 2.2(2xm, 2x1H,=$CCH_2$), and 1.8(s,6H,2xMe); m/z(%) 287(20), 217(100) and 90(58).

**2-(2′-Iodo-N-phenylsulphonylanilinyl)-4-azaphenylsulphonyl-6-methylhepta-1,6-diene(30).**

(i) A solution of N-phenylsulphonyl-2-iodoaniline (3.59g, 0.01mol) in dry DMF(50ml) was stirred whilst sodium hydride (0.5g, 50% in mineral oil) was added portionwise. The mixture was stirred a further 1h and then 2-chloromethyl-3-chloropropene (2.5g, 0.02mol) was added dropwise over 5min. After stirring at room temperature overnight the mixture was worked up in the usual way to afford 2-(2′-iodo-N-phenylsulphonylanilinyl)-3-chloropropene(2.57g, 58%) as colourless needles from ether-petroleum ether, m.p. 90-91°C (Found: C, 42.75; H, 3.35; N, 3.2. $C_{16}H_{15}ClINO_2S$ requires C, 42.9; H, 3.35; N, 3.15%); δ 7.9-6.9(m, 9H, ArH), 5.2 and 4.8(2xs, 2x1H,=$CH_2$), 4.5 and 4.25(2xd, 2x1H, $NCH_2$), and 4.35 and 4.15(2xd, 2x1H,$CH_2$); m/z(%) 447($M^+$,11), 412(14), 320(49), 306(38), 179(12) and 144(83).

(ii) Sodium hydride (0.24g, 50% in mineral oil) was added portionwise to a stirred solution of N-phenylsulphonyl methallylamine (1.05g, 0.005mol) in dry DMF(30ml). The mixture was stirred for 1h and then a solution of 2-(2′-iodo-N-phenylsulphonylanilinyl)-3-chloropropene (2.33g, 0.005mol) in dry DMF(10ml) was added dropwise over 15min. and stirring continued for a further 14h. The resulting mixture was worked-up in the usual way. Flash chromatography eluting with 1:1v/v ether-petroleum ether afforded the product (1.6g, 52%) which crystallised from ether-petroleum ether as colourless needles, m.p. 85-86°C (Found: C, 50.25; H, 4.3; N, 4.5. $C_{26}H_{27}IN_2O_4S_2$ requires C, 50.15; H, 4.35; N, 4.5%); δ 7.9-6.9(m, 14H, ArH), 4.9(s, 2H, = $CH_2$), 4.75 and 4.65(2xs, 2x1H,= $CH_2$) 4.2 and 3.95(2xd, 2H, $NCH_2$), 3.9(br s,2H, $NCH_2$), 3.7(dd, 2H, $NCH_2$), and

1.5(s,3H,Me); m/z(%)(CI) 640($M+NH_4^+$,70), 623(20), 434(100), 355(68) and 160(5).

**2-Bromo-4-N-phenylsulphonylmethallylaminobicyclo[3.2.1]oct-2-ene(36).** Sodium hydride (1.0g, 50% in mineral oil) was added portionwise to a stirred ice cooled solution of N-phenylsulphonylmethallylamine(4.16g, 0.02mol) in dry DMF(50ml). The mixture was stirred for 1h and then a solution of 3,4-dibromobicyclo[3.2.1]oct-2-ene(5.22g, 0.02mol) in DMF(20ml) was added dropwise and the resulting mixture heated to 78°C for 2h. Work-up in the usual way afforded the product (5.6g, 80%), which crystallised from ether-petroleum ether as colourless prisms, m.p. 120-122°C (Found: C, 54.6; H, 5.7; N, 3.6. $C_{18}H_{22}BrNO_2S$ requires C, 54.55; H, 5.55; N, 3.55%); δ 8.0-7.4(m, 5H,ArH), 6.4(d, 1H,=CH), 5.2 and 5.0(2xs, 2x1H,=$CH_2$), 4.1(d, 1H, NCH), 4.0(s, 1H,=CCHN), 3.4(d, 1H, NCH), 2.9 and 2.5(2xbr s, 2x1H), 2-1.2(m, 6H,3x$CH_2$), and 1.8(s,3H,Me); m/z(%) 397/395($M^+$,9), 356/354(4), 316(100), 254(25), 174(35) and 77(95).

**Allylic Acetate(38).** Prepared from 1-acetoxy-4-chlorocyclohex-2-ene and dimethyl methallylmalonate by the same procedure as that described above. The product (76%) was obtained as a thick colourless oil after purification by column chromatography (Found: C, 62.6; H, 7.1. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.45%); δ 5.86 and 5.54(2xd, 2x1H, J 10.5Hz, CH=CH), 5.19(br s, 1H, CHOAc), 4.77 and 4.64(2xs, 2x1H,=$CH_2$), 3.64 and 3.16(2xs, 2x3H, 2xOMe), 2.92(br s, 1H, C<u>H</u>-CH=), 2.65(dd,2H,$CH_2$), 1.97 and 1.62(2xs, 2x3H, OCOMe and =CMe), and 2.0 and 1.4(2xm, 2x2H,2x$CH_2$); m/z(%) 325(M+1,16), 265(87), 205(85), 176(58), 145(100), 96(58), 79(68) and 43(83).

**N-Benzyl-N-(buta-1'3'-dienyl)-2-iodobenzamide(42).** A solution of 2-iodobenzoyl chloride (13.38g, 0.05mol) in dry benzene(30ml) was added dropwise to a stirred ice cooled solution of the benzylamine imine of crotonaldehyde (7.95g, 0.05mol) and N,N-diethylaniline (8.21g, 0.55mol) in dry benzene(100ml). The resulting mixture was stirred at room temperature for a further 15h, filtered, and the filtrate evaporated under reduced pressure. The residue was purified by flash chromatography eluting with 1:3v/v ether-petroleum ether to afford the product (11.5g, 59%) as a pale yellow thick oil (Found: C, 55.8; H, 3.9; N, 3.7. $C_{18}H_{16}INO$ requires C, 55.55; H, 4.15; N, 3.6%); δ 7.88(dd, 1H, ArH), 7.47-7.02(m,8H,ArH), 6.41(d,1H, CH=C<u>H</u>N), 5.99(m,1H, CH=C<u>H</u>), 5.73(dd,1H, C<u>H</u>=CHN), 5.10 and 5.09(2xs, 2H, $NCH_2$), and 4.98 and 4.87(2xdd, 2H,C<u>H</u>$_2$=CH); m/z(%) 389($M^+$,41), 231(100), 203(16) and 91(43).

**Dienylamide(44).**

(i) Verbenone and benzylamine were boiled under reflux in dry benzene, using a Dean-Stark apparatus, to afford the corresponding benzylamine imine (81%) as a colourless oil, b.p. 118-122°C/0.2mmHg. The imine darkens on storage (Found: C, 85.15; H, 8.65; N, 5.55. $C_{17}H_{21}N$ requires C, 85.3; H, 8.85; N, 5.85%). The p.m.r. spectrum of the imine showed it comprised a mixture of syn- and anti-isomers. δ 7.27(m,5H, ArH), 6.21 and 5.9(2xbr s,1H, C<u>H</u>=CMe), 4.64 and 4.56 (s and d, 2H, $NCH_2$), 3.28 and 2.80(2xbr t, 1H), 2.7(m,1H), 1.95 and 1.9(2xbr s, 3H,=CMe), 2.3 and 1.77(2xm, 2x1H,$CH_2$) and 1.43, 0.93 and 0.86(3xs, 6H, 2xMe); m/z(%) 240(M+1,3), 238(13), 159(19), 92(10) and 91(100).

(ii) A solution of 2-iodobenzoyl chloride (5.32g, 0.02mol) in dry benzene (15ml) was added dropwise with stirring to a solution of the imine (4.78g, 0.02mol) and triethylamine(2.02g, 0.02mol) in dry benzene (60ml). The resulting mixture was boiled under reflux for 2h, cooled, filtered, and the filtrate evaporated to dryness. The residue was purified by flash chromatography eluting with 2:3 v/v ether-petroleum ether to afford the product (6.0g,65%) as colourless prisms from ether-petroleum ether, m.p. 128-129°C (Found: C, 61.3; H, 5.3;

N, 3.15. $C_{29}H_{29}INO$ requires C, 61.4; H, 5.15; N, 3.0%); δ 7.79(d,1H,ArH), 7.33(m,7H,ArH), 7.0(dt, 1H,ArH), 5.85(br s, 1H, CH=CN), 5.10(d,1H, NCH), 4.62(m,3H,=$CH_2$ and NCH), 2.34(br s, 1H), 2.23(m,2H), 1.2 and 0.42(2xbr s, 2x3H, 2xMe), and 0.58(br d, 1H); m/z(%) 469($M^+$,37), 231(86), 203(19), 91(100) and 86(58); $\upsilon_{max}$(KBr) 3000, 2962, 1627, 1393, 1331, 751, 741 and 699$cm^{-1}$.

**9-(2′-Bromoprop-2-enyl)-9-(2′,4′-pentadienyl)fluorene(47).**

(i) n-Butyl lithium (8.5ml of a 1.6M solution in hexane, 0.013mol) was added to a stirred and cooled (-78°C) solution of fluorene (2.1g, 0.127mol) and HMPA(2.5ml) in dry THF(50ml) under an atmosphere of dry nitrogen. After stirring for 15min., a solution of 1-bromopenta-2,4-diene (1.9g, 0.129mol) in THF(20ml) was added dropwise and the mixture stirred for a further 15 min. at -78°C and then allowed to warm to room temperature. Work up in the usual way afforded 9-(2′,4′-pentadienyl) fluorene (2.6, 88%) as a pale yellow viscous oil which was used in the next step without further purification.

(ii) In a manner analogous to that described above, 9-(2′,4′-pentadienyl) fluorene (2.6g) n-butyl lithium (8ml of 1.6M solution in hexane) and 2,3-dibromopropene(2.5g) in dry THF(50ml) afforded the product (2.1g, 53%) as a viscous colourless oil after column chromatography ($Al_2O_3$) eluting with ether (Found: C, 72.05; H, 5.65; Br, 22.4. $C_{21}H_{19}Br$ requires C, 71.8; H, 5.45; Br, 22.75%); δ 7.7-7.36(m, 8H, ArH), 6.07(m, 1H,=CH), 5.88(br t, CH=CHCH), 5.21(dd, 1H,=CHC$H_2$), 5.06 and 4.84(2xbr s, 2H, C(Br)=$CH_2$), 4.92(m, 2H, CH=$CH_2$), 3.2(br s, 2H, $CH_2$CBr) and 2.7(d, 2H,=C$CH_2$); m/z(%) 352(6), 285(70), 283(66), 215(28), 203(100) and 165(76); $\upsilon_{max}$(film) 3066, 2919, 1623, 1477, 1260, 893, 765 and 735 $cm^{-1}$.

**Diethyl 2-bromoprop-2-enyl(2′,4′-pentadienyl)malonate(49).** Diethyl 2-bromoprop-2-enyl malonate (3.7g, 0.133mol) in dry ethanol (5ml) was added dropwise with stirring over 5min. to ethanolic sodium ethoxide [from Na(0.32g, 0.139mol) and ethanol (50ml)] under a nitrogen atmosphere. The mixture was stirred for 15min. and then 1-bromopenta-2,3-diene (2g, 0.136mol) was added and stirring continued for a further 14h. Work up in the usual way afforded the product (2.9g, 62%) as a colourless oil (Found: C, 52.0; H, 6.3; Br, 23.2. $C_{15}H_{21}BrO_4$ requires C, 52.2; H, 6.15; Br, 23.15%); δ 6.3(m, 1H, CHCH=$CH_2$), 6.13 (q, 1H, C=CH-CH=), 5.7 and 5.6(2xt, 2x1H, C(Br)=$CH_2$), 5.54(m, 1H, $CH_2$CH=$CH_2$), 4.22(m, 2x2H, O$CH_2$Me), 3.17(s, 2H, $CH_2$CBv), 2.88(d, 2H, C$H_2$CH=C), and 1.28(t, 6H, $CH_2$Me); m/z(%) 346/344($M^+$,3), 267(11), 259(11), 191(48), 180(11), 179(100), 133(13) and 91(27); $\upsilon_{max}$(film) 3045, 2940, 1625, 1465, 973 and 801 $cm^{-1}$.

**Palladium Catalysed Cyclisation - Hydride Capture.**

**General Procedure.**

*(i) Catalyst System A.* A mixture of iodo- or bromo- substrate (2mmol), palladium acetate (0.2mmol), triphenylphosphine(0.4mmol), tetraethylammonium chloride (2mmol), and sodium formate (2.2mmol) in DMF (25ml) was stirred and heated at 80-100°C under a nitrogen atmosphere until tlc monitoring showed that all the starting material had been consumed. The mixture was cooled, filtered, and the filtrate evaporated under reduced pressure. The residue was dissolved in ether and filtered through a short silica column eluting with ether. Evaporation of the eluate followed by crystallisation or preparative tlc, as appropriate, afforded the product.

*(ii) Catalyst System B.* The same as system A but with acetonitrile as solvent and a reaction temperature of 80°C.

*(iii) Catalyst System C.* The same as system A but with the tetraethylammonium chloride and sodium formate replaced by formic acid(6mmol) and piperidine(8mmol).

*(iv) Catalyst System D.* The same as system A but omitting the tetraethylammonium chloride.

**3,3-Dimethyl oxindole(6a).** Prepared using catalyst system B and a reaction line of 24h. Purification by preparative tlc eluting with 7:3 v/v ether-petroleum ether afforded the product(65%) which crystallised from ethyl acetate as colourless prisms, m.p. 152-153°C. (Found: C, 74.4; H, 6.9; N, 8.65. $C_{10}H_{11}NO$ requires C,74.5; H, 6.9; N, 8.7%); δ 9.05(br s, 1H,NH), 7.17(m,4H,ArH) and 1.41(s,6H, 2xMe); m/z(%) 161($M^+$,81), 146(100), and 91(10); $\upsilon_{max}$(KBr) 3432, 3151, 2966, 1710, 1673, 1383 and 1250cm$^{-1}$.

**N-Benzyl-3,3-dimethyl oxindole(6b).** Prepared as above with a reaction time of 12h. Preparative tlc eluting with 9:1v/v ether-petroleum ether followed by crystallisation from ethanol afforded the product(80%) as colourless prisms, m.p. 73-76°C (Found: C, 81.65; H, 7.05. $C_{17}H_{17}NO$ requires C, 81.65; H, 7.1%); δ 7.25(m, 8H, ArH), 6.71(d, 1H,ArH), 4.92(s,2H,$NCH_2$), and 1.44(s,6H,2xMe); m/z(%) 251($M^+$,100), 236(17), 209(1) 160(11), 146(3) and 91(95); $\upsilon_{max}$(KBr) 3055, 2966, 1710 and 1653cm$^{-1}$.

**N-Benzyl-3,3-dimethyl-4-azaisoindoline-1-one(8).** Prepared using catalyst system A at 120°C for 16h. the product(54%) crystallised from ether-petroleum ether as colourless needles, m.p.60°C. Found: HRMS 252. 1262. $C_{16}H_{16}N_2O$ requires 252.1258. δ 8.58 and 8.0(2xm, 2x1H,ArH), 7.3-7.1(m,6H,ArH), 4.67(s,2H,$NCH_2$), and 1.3(s,6H,2xMe); m/z(%) 252($M^+$,23), 239(20), 91(53) and 84(100).

**Cyclisation products (10a) and (11a)** Prepared using catalyst system D with a reaction time of 24h. Work-up followed by preparative tlc eluting with 1:3 v/v ether-petroleum ether afforded a 2:1 mixture of (10a) and (11a).
**(10a).** Colourless prisms, m.p. 82-85°C from ether-petroleum ether. Found: HRMS 249.1154. $C_{17}H_{15}NO$ requires 249.1153. δ 7.52(m,8H,ArH), 4.63 and 3.39 (2xm,$CH_2N$), 3.11 and 2.8(dd and m, 2x1H, $CH_2CH_2N$) and 1.83(s,3H,Me); m/z(%) 249($M^+$,8), 247(8), 246(17), 234(15), 233(100) and 231(15).
**(11a).** Identical physical and spectroscopic properties to that described previously.[24]
**Spirocycle(15).** Prepared using catalyst system B with a reaction time of 18h. Work-up followed by preparative tlc eluting with 4:1 v/v ether-petroleum ether afforded the product (45%) as pale yellow plates from ether-petroleum ether, m.p. 132-133°C. Found: HRMS 347.2236. $C_{24}H_{29}NO$ requires 347.2249. δ 7.8-7.2(m,9H,ArH), 4.8(br s, 2H, $NCH_2$), 2.0, 1.6 and 1.4(3xd, 3x2H,3x$CH_2$), and 1.2 and 0.9(2xs, 2x6H, 4xMe); m/z(%) 347($M^+$,70), 332(11), 276(100), 91(89) and 84(68).
**Spirocycle(19a).** Prepared using catalyst system C with a reaction time of 2.5h. After preparative tlc eluting with 3:7 ether-petroleum ether the product (65%) crystallised from ether-petroleum ether as colourless prisms, m.p. 130°C (Found: C, 82.9; H, 7.05; N, 4.5. $C_{21}H_{22}NO$ requires C, 83.15; H, 7.0; N, 4.6%); δ 7.73-7.0(m,9H,ArH), 4.95 and 4.59(2xd, 2x1H, $NCH_2$), 2.35(br s,1H), and 2.13-1.22(m,9H); m/z(%) 303($M^+$,69), 234(20), 212(28) and 105(100).
**Spirocycle(19b).** Prepared using catalyst system A and a reaction time of 5h. The product(66%) crystallised from ether-petroleum ether as colourless needles, m.p. 114°C (Found: C, 78.85; H, 6.6; N, 9.5. $C_{20}H_{20}N_2O$ requires C, 79.15; H, 6.3; N, 9.25%); δ 8.7 and 8.0(2xdd, 2x1H,ArH), 7.3(m,6H,ArH), 4.96 and 4.76(2xd, 2x1H,$NCH_2$), 3.1(d,1H), 2.5(br s, 1H), 2.2(d,2H,$CH_2$), and 1.8-1.3(m,6H,3x$CH_2$); m/z(%) 304($M^+$,83), 237(53), 213(90) and 91(100).
**Spirocycle(22).** Prepared using catalyst system B and a reaction time of 20h. The product (55%) crystallised from methanol as colourless prisms, m.p. 124-126°C. (Found: C, 77.4; H, 7.25; N, 3.45. $C_{26}H_{29}NO_3$ requires C, 77.3; H, 7.25; N, 3.45%); δ 7.91(d,1H,ArH), 7.59(m,2H,ArH), 7.46(m,1H,ArH), 7.21(m,5H,ArH), 5.32(q,

2H,$NCH_2$), 3.73(s,3H,OMe), 2.61(dd,1H), 2.43(m,1H), 1.83, 1.72 and 1.55(3xm,3x2H,3x$CH_2$), 1.22(m,1H), 0.95(s,3H,Me) and 0.4(d,3H,Me); m/z(%) 403($M^+$,48), 312(10), 262(3), 236(100), 168(19) and 91(91); $\upsilon_{max}$(KBr) 3024, 2959, 2918, 1714, 1696 and 1667$cm^{-1}$.

**Spirocycle(25)(with Dr. P. Ratananukul).** Prepared using catalyst system C but with acetonitrile as solvent and a reaction time of 4.5h. The product (68%) was obtained as a colourless solid by preparative tlc eluting with methylene chloride, m.p. 159-160°C. (Found: C, 88.35; H.7.15; N, 5.9. $C_{22}H_{21}NO$ requires C, 88.25; H, 7.05; N, 4.7%); δ 7.7 and 7.58(2xm, 2x1H, ArH), 7.48-7.17(m,7H,ArH), 6.54 and 6.44 (m and dd, 2x1H, CH=CH), 4.89(d, 2H,$NCH_2$), 2.83 and 2.42 (2xm,2x1H) and 1.96-1.12(m,6H,2xMe); m/z(%) 315($M^+$,52), 236(100) and 91(47); $\upsilon_{max}$(KBr) 3050, 2953, 1687, 1464 and 1355$cm^{-1}$

**Compound (27a).** Prepared using catalyst system B and a reaction time of 16h. Purification by preparative tlc eluting with 1:1 ether-petroleum ether, followed by crystallisation from ethanol afforded the product (60%) as colourless needles, m.p. 149-151°C (Found: C, 82.05; H, 6.95; N, 4.75. $C_{19}H_{19}NO$ requires C, 82.25; H, 6.9;N, 5.05%); δ 7.69(d,1H,ArH), 7.25(m,8H,ArH), 3.93 and 3.1(2xd, 2x1H,$NCH_2$), 2.63 and 1.95(2xd, 2x1H,$CH_2$), and 1.05 and 0.95(2xs, 2x3H,2xMe), m/z(%) 277($M^+$,100), 276(4), 221(43), 200(17), 193(5) and 165(14); $\upsilon_{max}$(KBr) 3018, 2452, 2864, 1683 and 755$cm^{-1}$.

**Compound (27b).** Prepared using catalyst system A and a reaction time of 6h. Work-up followed by preparative tlc eluting with 2:3v/v ether-petroleum ether afforded the product (70%) as a colourless oil (Found: C, 78.25; H, 8.2; N, 6.6. $C_{14}H_{17}NO$ requires C, 78.1; H, 7.95; N, 6.5%); δ 7.8-7.4(m, 4H,ArH), 3.89 and 3.10(2xd, 2x1H, $NCH_2$), 1.80(AB quartet, 2H, $NCH_2$), 1.53, 1.23 and 0.83(3xs,3x3H, 3xMe); m/z(%) 215($M^+$,55), 200(34), 159(100), 130(26), 103(6), 91(3), 90(4) and 77(3).

**Compound (29a)** Prepared using catalyst system B, but without tetraethylammonium chloride, and with a reaction time of 36h. Purification by preparative tlc eluting with 1:1v/v ether-petroleum ether afforded the product (70%) as a colourless oil (Found: C, 80.5; H, 8.85. $C_{25}H_{20}O$. $0.5H_2O$ requires C, 80.0; H, 8.97%); δ 7.2-6.8(m,4H,ArH), 4.6(dd,2H,$OCH_2$), 3.8(br d,1H, OCH), 2.0(dd,2H,$CH_2$),1.75(t,2H,$CH_2$), and 1.2, 1.1 and 1.0(3xs, 3x3H, 3xMe); m/z(%) 216($M^+$,50), 145(100), 117(30) and 91(32).

**Compound (31a).** Prepared using catalyst system A but with thallium(1) carbonate (2mol) replacing tetraethylammonium chloride. The reaction was carried out for 48h at 80°C. Work-up afforded a residue which comprised (p.m.r.) a 4:1 mixture of (31a) and (32). Preparative tlc eluting with 1:1v/v ether-petroleum ether afforded the product (40%) as colourless needles from ether-petroleum ether, m.p. 252-255°C(d), Found: HRMS 496.1491. $C_{26}H_{28}N_2O_4S$ requires 496.1490. δ 8-6.8(m, 14H,ArH), 4.5 and 3.8(2xd, 2x1H,$NCH_2$), 3.5 and 2.0(2xd,2x1H,$NCH_2$), 3.2 and 1.9(2xd,2x1H,$NCH_2$), 1.5(2xd,2H,$CH_2$) and 1.1 and 0.9(2xs,2x3H,2xMe); m/z(%)(CI) 514 ($M+NH_4^+$,15), 497(M+1,50), 357(100), and 130(52).

**Compound (37).** Prepared using catalyst system A at 80°C and a reaction time of 18h. Work-up in the usual way followed by column chromatography eluting with 1:4v/v ether-petroleum ether afforded the product (74%) which crystallised from ether-petroleum ether as pale yellow prisms, m.p. 109-111°C. (Found: C, 68.0; H, 7.25; N, 4.3. $C_{18}H_{23}NO_2S$ requires C, 68.15; H, 7.25; N, 4.4%); δ 8-7.6(m,5H,ArH), 5.96(d,1H,J 9.5Hz,=CH), 3.4(s,1H,=CCHN), 3.2(br d, 2H,CH and NCH), 2.96(d,1H, J 10.6Hz, NCH), 2.5(br s, 1H), 2.0-1.0(m,6H, 3x$CH_2$), and 0.98 and 0.35(2xs, 2x3H, 2xMe); m/z(%) 317($M^+$,25), 302(98), 276(100), 176(36), 154(54),

148(23), 141(20) and 91(32).

**Compound (40a).** Formic acid (0.32g, 0.005mol) was added over 5 min to a stirred solution of allylic acetate (38)(0.324g, 0.001mol), palladium acetate (0.020g, 10mol%) and triphenylphosphine(0.052g, 20mol%) in acetonitrile (10ml). The resulting mixture was stirred and heated under reflux for 19h. Work-up followed by column chromatography eluting with 1:19v/v ether-petroleum ether afforded the product (0.17g, 64%), which crystallised from ether-petroleum ether as colourless prisms, m.p. 55-57°C (Found: C, 67.65; H, 8.5. $C_{15}H_{22}O_4$ requires C, 67.65; H, 8.3%); δ 5.67 and 5.47(2xm, 2x1H, CH==CH) 3.68 and 3.65(2xs, 2x3H, 2xOMe), 2.84(m,1H), 2.47 and 2.04(2xd, 2x1H, $CH_2$), 2.06-1.62(m,3H), 1.28-1.16(m,2H), and 0.94 and 0.89(2xs, 2x3H, 2xMe); m/z(%) 266($M^+$,21), 206(69), 191(51), 147(66), 145(100), 132(79), 122(71), 113(60), 91(60) and 79(61).

**Compound (43).** Prepared using catalyst system C but with acetonitrile as solvent and with a reaction time of 3h. Work-up followed by preparative tlc afforded the product (67%) as a pale yellow oil whose pmr spectrum showed it to comprise a 2:1 mixture of E- and Z- isomers. Found: HRMS 263.131 $C_{18}H_{17}NO$ requires 263.131. m/z(%)(mixture) 263($M^+$,65), 172(28), 159(41), 131(27) and 91(100); δ(E- isomer) 8.79(m,1H,ArH), 7.5(m,2H,ArH), 7.25(m,7H,ArH), 5.8(m,1H,=CHMe), 5.2 and 4.0(2xd, 2x1H, $NCH_2$), 5.0(m,1H,=CH), 4.6(d,1H,ArCH), and 1.8(d,3H,Me); δ(Z- isomer) 5.25 and 3.9(2xd, 2x1H, $NCH_2$), and 1.5(d,3H,Me). The remaining signals overlap with those of the E- isomer.

**Compounds (45) and (46).** Prepared using catalyst system D and a reaction time of 24h. Work-up followed by column chromatography ($AlO_3$) eluting with 1:1v/v ether-methylene chloride afforded the product (59%) as a 4:1 mixture of (45) and (46). Fractional crystallisation from methylene chloride afforded **(45)** as colourless rods, m.p. 145-147°C. Found: HRMS 343.1936. $C_{24}H_{25}NO$ requires 343.1936. The minor isomer (46) was not isolated and its pmr data (below) is abstracted from the spectrum of a mixture with (45). m/z(%) (mixed isomers) 343($M^+$,38), 328(5), 300(7), 248(18) and 91(100); $\upsilon_{max}$(KBr) (mixed isomers) 3002, 2948, 1693, 1464, 1100 and 831$cm^{-1}$.

**(45).** δ 7.45(m, 9H,ArH), 5.31 and 4.54(2xd, 2x1H, $NCH_2$), 4.81 and 4.68(2xbr s, 2x1H,=$CH_2$), 3.12 and 2.60(2xbr d, 2x1H,=$CCH_2$), 2.49(m,2H,=CCH and 1H of $CHCH_2CH$), 2.06(m,2H,$CHCH_2$ and 1H of $CHCH_2CH$), and 1.28 and 1.17(2xs, 2x3H, 2xMe).

**(46).** 7.52(m,9H,ArH), 5.16 and 4.84(2xd, 2x1H, $NCH_2$), 5.10(br s, 1H,=CH), 2.54(m,1H, 1H of $CHCH_2CH$), 2.39(d,1H,=CCH), 2.06(m,2H,1H of $CHCH_2CH$ and $CHCH_2$), 1.78(br s, 3H,=CMe), and 1.32 and 1.11(2xs, 2x3H, 2xMe).

**Compound (48).** Prepared using catalyst system C but with acetonitrile as the solvent and pyrrolidine as the base with a reaction time of 19h. Work-up followed by preparative tlc eluting with 1:3v/v ether-petroleum ether afforded the product (90%) as a bright yellow oil which comprised a 1:1 mixture of E- and Z- isomers, b.p. (molecular distillation) 105°C (furnace temp.)/0.05mmHg (Found: C, 92.9; H, 8.1. $C_{21}H_{20}$ requires C, 92.6; H, 7.4%); δ 7.46(m,8H,ArH), 5.85 and 5.55(m,1H, E- and Z- CH=CHMe), 5.05(m,3H, CH=CHMe and =$CH_2$), 2.83(m,3H, =$CCH_2$ and $CHCH_2$), 2.11(m,2H,$CHCH_2$), and 1.75(m,3H,Me); m/z(%) 272($M^+$,97), 231(42), 217(29), 178(100), and 165(41); $\upsilon_{max}$(film) 3065, 2917, 1447, 1377, 1100, 884 and 760$cm^{-1}$.

**Compound (50).** Prepared using catalyst system C but with acetonitrile as the solvent and with pyrrolidine replacing piperidine as the base. Work-up after 6h followed by preparative tlc eluting with 1:9 v/v ether-

petroleum ether afforded the product (77%) as a colourless liquid which comprised a 1:1 mixture of E- and Z-isomers (pmr), b.p.(molecular distillation) 65-70°C (furnace temp.)/0.3mmHg (Found: C, 68.55; H, 8.5. $C_{16}H_{24}O_4$ requires C, 68.55; H, 8.65%); δ 5.45(m,2H,CH=CH), 4.96(m,2H,=$CH_2$), 4.18(m,4H, 2x$CH_2$Me), 3.0(m,2H,=$CCH_2$), 2.70 and 2.51(2xm, 2x1H,=CHC$H_2$), 2.31(m,1H,C$H$C$H_2$), 2.0 and 0.95(2xm,2x1H,$CH_2$), 1.64(m,3H,Me) and 1.24(m,6H,2x$CH_2$Me); m/z(%) 280($M^+$,41), 206(100), 177(16), 105(15), and 91(24); $\upsilon_{max}$(film) 3076, 2981, 1733, 1657 and 861$cm^{-1}$.

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