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Palladium Catalysed Tandem Cyclisation - Anion Capture Processes. Part 2.[1] Cyclisation onto Alkynes or Allenes with Hydride Capture.

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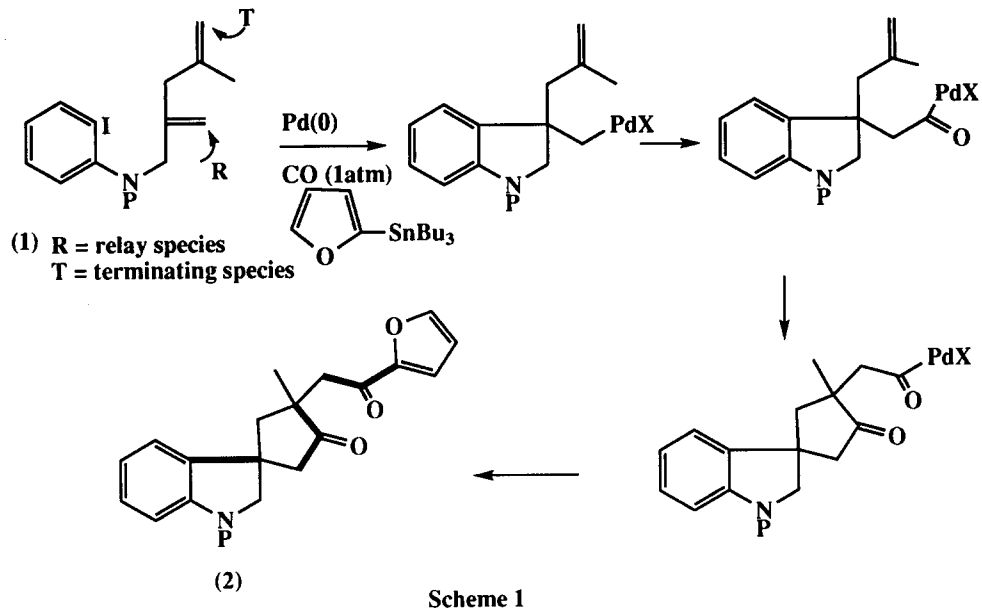
Abstract: A wide range of palladium catalysed regio- and stereo-specific 5-, 6- and 7-exo-dig mono-, bis- and tris-cyclisation processes of aryl and vinyl halides and allylic acetates are described. The mono- and bis-cyclisation processes terminate in hydride capture from piperidine-formic acid or sodium formate. Addition of Tl_2CO_3 results in alkyne-allene isomerisation and leads, after cyclisation, to 1,3-dienes which give Diels-Alder adducts in good yield.

In the first paper in this series we outlined the background to our novel palladium catalysed tandem cyclisation-anion capture methodology and the potentially wide scope of these invariably regio- and stereo-specific processes.[1,2] In the intervening period the scope of the original 2-component cascade concept has been considerably widened with the achievement of polycomponent cascades.[3,4] A typical illustrative 4-component cyclisation-anion capture cascade involving the formation of five new C-C bonds is (1) → (2) (new C-C bonds are shown in bold) (Scheme 1).[5] An additional starter species, allenyl, has also recently been implemented[6] and is generated *in situ* from a propargylic carbonate.[7]

The increased scope of the methodology is emphasised by Table 1 which incorporates the, as yet little explored, polycyclisation-anion capture strategy.[8]

The range of anion transfer agents (Y) and combinations (Y/Z) thereof appears capable of significant further extension. In its expanded scope the starter species [halide, triflate or acetate (allyl starters)] undergoes oxidative addition to give an organopalladium(II) intermediate. In monocyclisation processes this intermediate then engages (intramolecular) the terminating species and the new organopalladium(II) species then completes the catalytic cycle by capture of Y or undergoes a sequential double capture of Y followed by Z. In polycyclisation processes the organopalladium(II) intermediate derived from the starter species initially engages a relay species and the reaction can continue in the relay phase for one two ,.....n cycles engaging a succession of different types of relay species before engaging the termination species followed by subsequent capture of Y or Y/Z. Moreover the relay phase can alternate between the various intramolecular relay species shown in Table 1 and an



Scheme 1

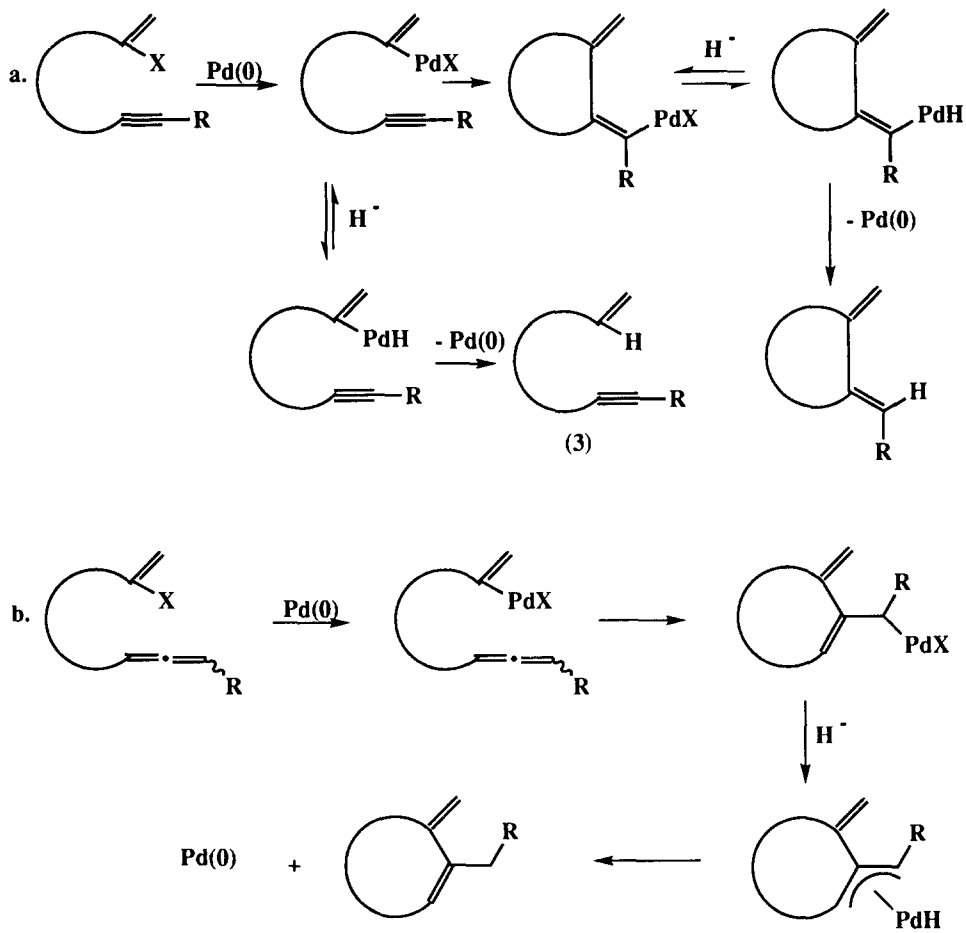
Table 1 Potential Combinations for Polymolecular (Poly) Cyclisation Anion-Capture Processes.

Starter Species	**Relay Species (R)**	**Terminating Species (T)**	**Y**	**Y/Z**
alkyl	alkene	alkene	**anionic** [H,OAc CN, SO_2Ph, $CH(CO_2R)_2$]	**neutral-anionic** CO/H˙,CO/ ˙$CH(CO_2R_2)$
aryl	alkyne	alkyne	**neutral** (amines, CO, acrylates)	**neutral-neutral** CO/ROH,CO/ amines, CO/
vinyl	1,2-diene	1,2-diene	**organometallics** RM[M=Sn(1V), B(111),Zn(11)]	alkene, allenes/amines **neutral-organometallics** CO/RM[M=Sn(1V), B(111)]
allenyl	1,3-diene	1,3-diene		

intermolecular relay species such as carbon monoxide. Such a relay switch is illustrated by Scheme 1 where the initial relay species is an alkene (intramolecular) followed by carbon monoxide (intermolecular) as a relay species, then an alkene (intramolecular) terminating species and finally capture by a neutral-organometallic Y/Z combination. The successful achievement of all the possible combinations inherent in Table 1 is predicated on the relative rates of all the possible reactions favouring the desired cascade. Our extensive experience to date with mono- and bis-cyclisation-anion captures and tri- and tetra-molecular cyclisation-anion capture queuing processes give cause for considerable optimism in this respect.

Part 1 in this series of papers was concerned with mono- and bis-cyclisations onto proximate alkenes and 1,3-dienes and capture of the resulting alkyl- or π-allyl-palladium(II) species by hydride ion. Sodium formate and

secondary amine-formic acid mixtures proved suitable hydride ion sources with the former generally preferred. This paper is concerned with cyclisation onto alkynes (Scheme 2a) and 1,2-dienes (Scheme 2b) followed by capture of the resulting vinyl- and π-allyl-palladium(II) species respectively by hydride ion.[9,10] In Scheme 2b the hydride capture can occur at either terminus of the π-allyl system but only one product is shown for brevity.



Scheme 2

A potential problem with all cyclisation-anion capture processes is operation of the shunt pathway, shown only in Scheme 2a for brevity, which leads to formation of (3) by replacement of X by H without cyclisation. Our experience of Table 1 (mono- and poly-cyclisations) to date indicates that when a cyclisation involves formation of 3 - 6 membered rings the shunt pathway is rarely a problem. However, in the few cases where the shunt pathway competes with cyclisation-anion capture the addition of Tl(I) salts[10,11] or tetraalkylammonium chlorides[12] invariably selectively enhances the rate of the desired cyclisation-anion capture.

The majority of the reactions described in this paper have employed one of the four catalyst systems noted below:

Catalyst A: 10 mol % $Pd(OAC)_2$, 20 mol % PPh_3, tetraethylammonium chloride (1 mol equiv.), formic acid (3 mol equiv.), piperidine (4 mol equiv.), MeCN as solvent.

Catalyst B: 10 mol % $Pd(OAc)_2$, 20 mol % PPh_3, tetraethylammonium chloride (1 mol equiv.), sodium formate (1.1 mol equiv.), MeCN as solvent.

Catalyst C: identical to catalyst A but without tetraethylammonium chloride.

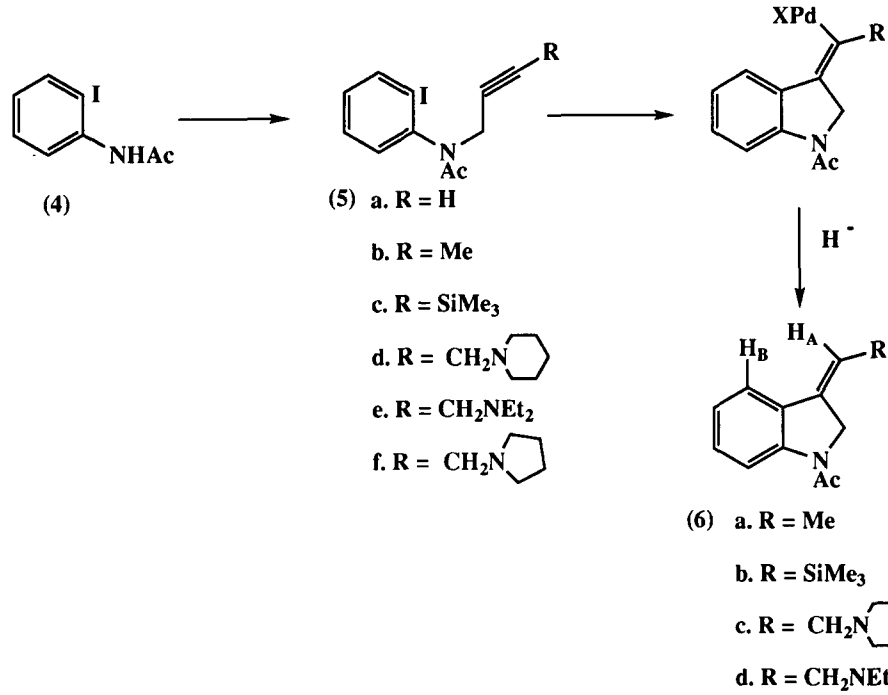
Catalyst D: identical to catalyst B but without tetraethylammonium chloride (1 mol equiv.).

No detailed studies of catalyst optimisation have been carried out.

The various cyclisation reactions are discussed in terms of the starter-terminating species combinations.

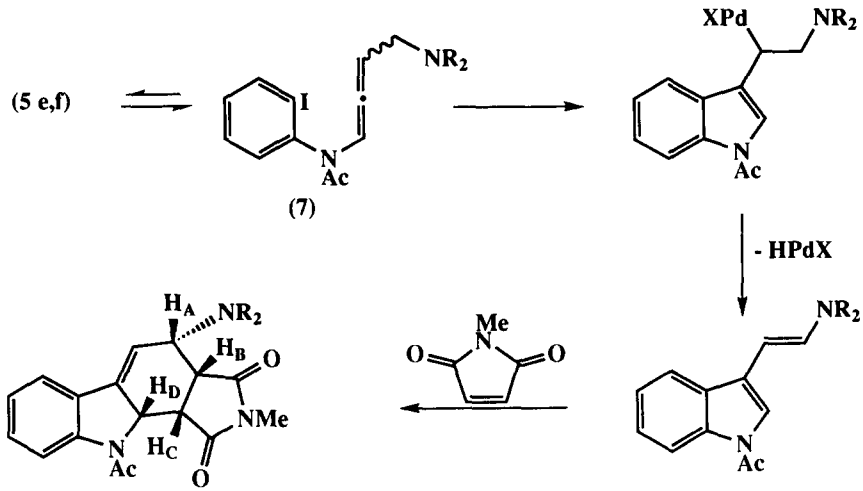
A. Aryl Halide Starter Species.

(i) 5-Exo-Dig Monocyclisations with Alkynes as Terminating Species. The aryl iodides (5a-c) were prepared from 2-iodo-N-acetylaniline (4) by alkylation at low temperature with the appropriate propargyl bromide using LDA as base. Subsequent Mannich reaction[13] of (5a) with formaldehyde and the appropriate dialkylamine furnished (5d-f) in 58-72% yield.



The disubstituted alkyne (5b) cyclised to (6a)(60%) at room temperature using a modified catalyst C without piperidine but with 1mol. equiv. of Ag_2CO_3. Alkyne (5c) cyclised to (6b)(50%) using catalyst A whilst (5d) and (5e) furnished (6c)(54%) and (6d)(56%) using catalyst D with the addition of Ag_2CO_3 (1 mol).[14] No products arising from direct hydride capture or from further reduction of (6a-d) were detected. The stereochemistry was established by n.O.e. studies and corresponds to the expected cis- addition of the intermediate arylpalladium(II) species to the alkyne. A typical example is provided by (6a), where irradiation of the vinylic proton H_A resulted in a 14% enhancement of the signal for the aromatic proton H_B together with a 10% enhancement of the signal for the vinylic methyl group.

(ii) 5-Exo-Dig Monocyclisations with Allenes as Terminating Species. Cyclisation of (5e,f) using catalyst D but with sodium formate (1.5 mol) and the addition of Tl_2CO_3 (1 mol) diverted the reaction into a new channel and produced the enaminoindoles (8a,b) which are believed to arise via alkyne-allene isomerisation (5) → (7) and regiospecific cyclisation onto the centre carbon atom of the allene moiety.[15,16] The enaminoindoles (8a,b) underwent cycloaddition to N-methylmaleimide (NMM) in boiling acetonitrile to afford the endo-cycloadducts (9a,b) in 56-60% overall yield from (5e,f).

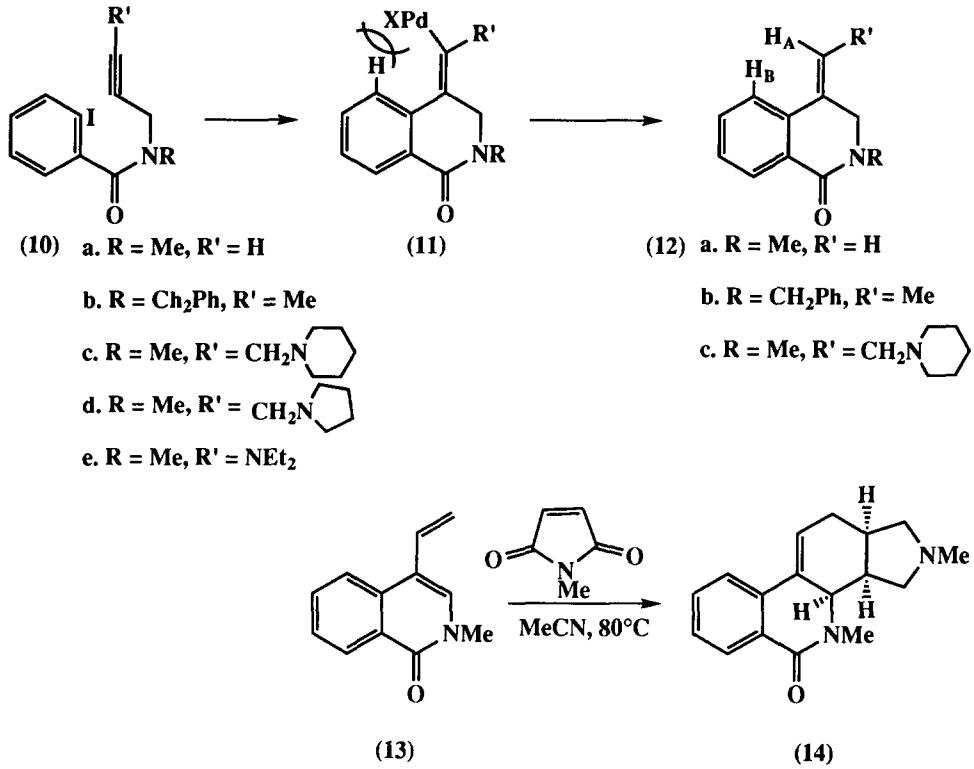


(9) **a.** R = Et
b. R = $(CH_2)_4$

The enaminoindoles (8a,b) were somewhat unstable and hence were not isolated but rather converted directly to the Diels-Alder cycloadducbts (9a,b). The stereochemistry of (9a,b) was established by n.O.e. studies. A typical example is provided by (9b). Thus irradiation of H_A effected enhancement of the signals for H_B (11%) and H_D (11%) whilst irradiation of H_C effected enhancement of the signals for H_B (14%) and H_D(10%). A more detailed study and discussion of the alkyne-allene isomerisation is provided below for related 6-exo-dig cyclisations.

(iii) 6-Exo-Dig Monocyclisations with Alkynes as Terminating Species. A series of 6-exo-dig cyclisation-hydride capture processes was studied next with substrates (10a-e). Compounds (10a,b) were prepared from reaction of 2-iodobenzoyl chloride with the appropriate N-alkylpropargylamine whilst (10c-e) were prepared from (10a) by the Mannich reaction.

The ^1H n.m.r. spectra of (10a-e) display the presence of rotational isomers about the amide bond. For example the room temperature spectrum ($CDCl_3$) of (10b) exhibits very broad signals for the two methylene groups attached to nitrogen. On raising the temperature to 73°C the broad signals are transformed into two sharp singlets at δ3.6($NCH_2C\equiv$) and 4.38(NCH_2Ph).

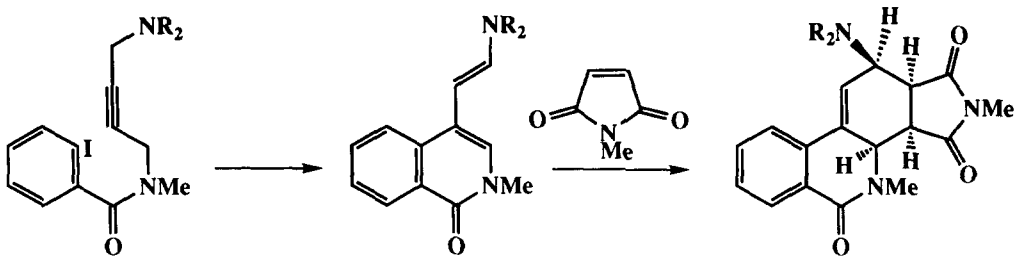


Iodoalkynes (10a) and (10b) are cyclised to (12a)(60%) and (12b)(50%) by catalyst A in acetonitrile at 60°C. No products arising from direct hydride capture or from further reduction of (12a,b) were detected. Initial attempts to effect cyclisation-hydride capture of (10c) using catalyst B gave a 2:1 mixture of (12c) and (13) in only 33% combined yield. The desired 6-exo-dig cyclisation-hydride capture product (12c) became the sole product (53%) when 1mol eq. of $TlNO_3$ was added to catalyst D. The stereochemistry of (12c) was established by n.O.e. studies. For example irradiation of H_A gave a positive n.O.e. on H_B of 18%.

Diene (13) was obtained as the sole product albeit in poor yield (32%) when (11c) was reacted with catalyst A at 60°C but without addition of piperidine. It underwent the expected Diels-Alder reaction with N-methylmaleimide in boiling acetonitrile to afford cycloadduct (14) in 80% yield.

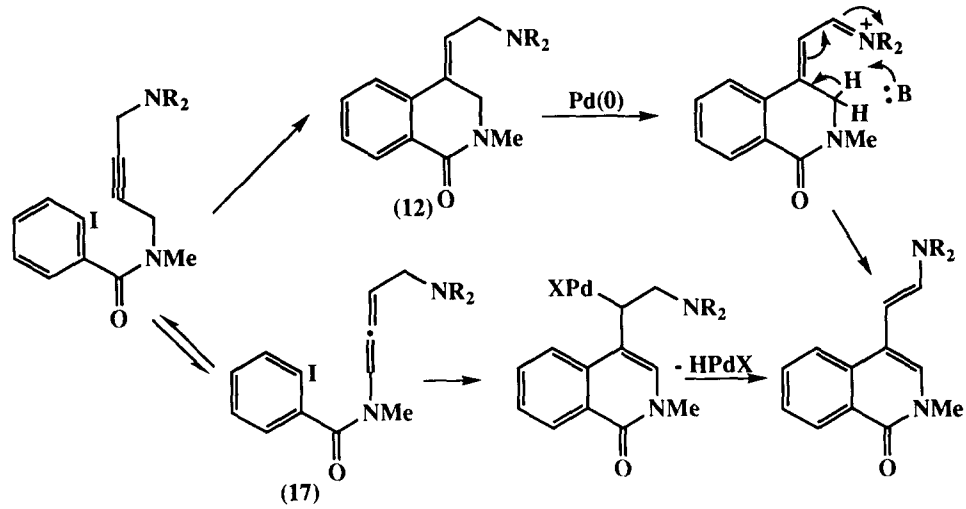
(iv) 6-Exo-Dig Monocyclisations with Allenes as Terminating Species. When (10c-e) were reacted with catalyst D together with 1mol eq. of Tl_2CO_3 (MeCN, 80°C) a different type of diene (15a-c) (Scheme 3) was produced in good yield.

The formation of (15a-c) is analogous to the conversion of (5d-f) → (8) discussed above. Although it was possible to isolate the dienes(15a-c) it was more convenient to add N-methylmaleimide after the cyclisation was judged complete by t.l.c. and allow the Diels-Alder reaction to occur (Scheme 3). Cycloadducts (16a-c) were obtained in 60-70% overall yield from (10c-e).



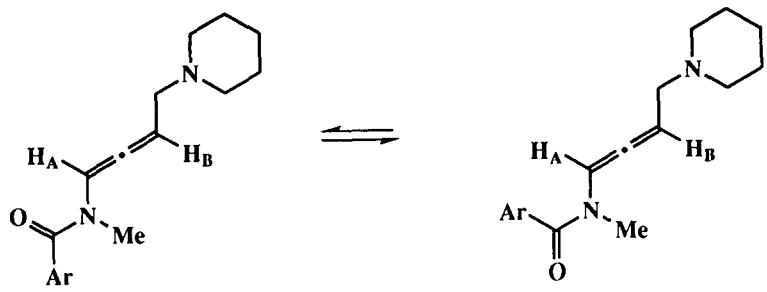
Scheme 3

Two mechanisms were considered for the formation of the dienes (15a-c) (Scheme 4).



Scheme 4

The dehydrogenation of t-amines to iminium species is known to occur with palladium catalysts[17] and hence the "normal" products (12) might give rise to (15) via such a process. However, recycling (12c) through the reaction failed to produce any diene (15b). Alkyne-allene isomerisation (10c-e) ⇌ (17) (Scheme 4) followed by cyclisation at the centre carbon atom of the allene and β-hydride elimination would also generate the dienes (15a-c). To test this hypothesis the alkyne (10c) was isomerised to allene [17, R_2=$(CH)_5$] by treatment with powdered NaOH in DMF. The proton n.m.r. spectrum of allene showed it to consist of a ca. 2.5:1 mixture of amide rotational isomers (17a) and (17b). The signals for H_A and the NMe group were particularly distinctive. When this allene was subjected to catalyst D it afforded the diene (15a) and subsequently the cycloadduct (16a) in good yield. Thus it might appear the more basic Tl_2CO_3 (compared to $TlNO_3$) effects the isomerisation of the alkynes to the allenes (17) and the cyclisation step is a 6-exo-dig process involving the central carbon atom of the allene. However, replacing both sodium formate and Tl_2CO_3 by thallium(I) formate also gave the dienes (15a-c) in good yield whilst in the absence of sodium formate but with Tl_2CO_3 the dienes (15a-c) were produced in low yield.



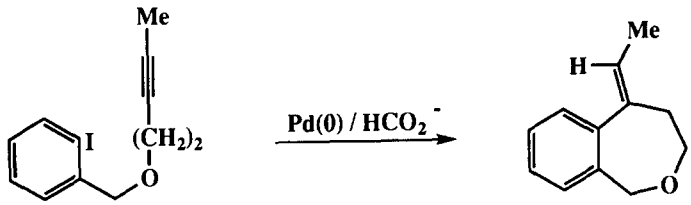
(17a) H_A, δ 7.65

NMe, δ 2.85

(17b) H_A, δ 6.4

NMe, δ 3.2

(v) 7-Exo-Dig Monocyclisation with Alkyne as Terminating Species. Substrate (18) was prepared from 2-iodobenzyl chloride and pent-3-yn-1-ol in 70% yield. Treatment of (18) with catalyst A in MeCN at 80°C for 16h afforded the desired product (19) (62%). A further example of a 7-exo-dig cyclisation-hydride capture process has recently been reported.[18]



(18) (19)

(vi) Bis-and Tris-cyclisation Processes. Two series of 2-iodo-N-(β,ω-dialkynyl) acetanilides/phenylsulphonanilides were prepared, as outlined in Scheme 5, as potential biscyclisation substrates involving alkyne relay and terminating species (Table 1).

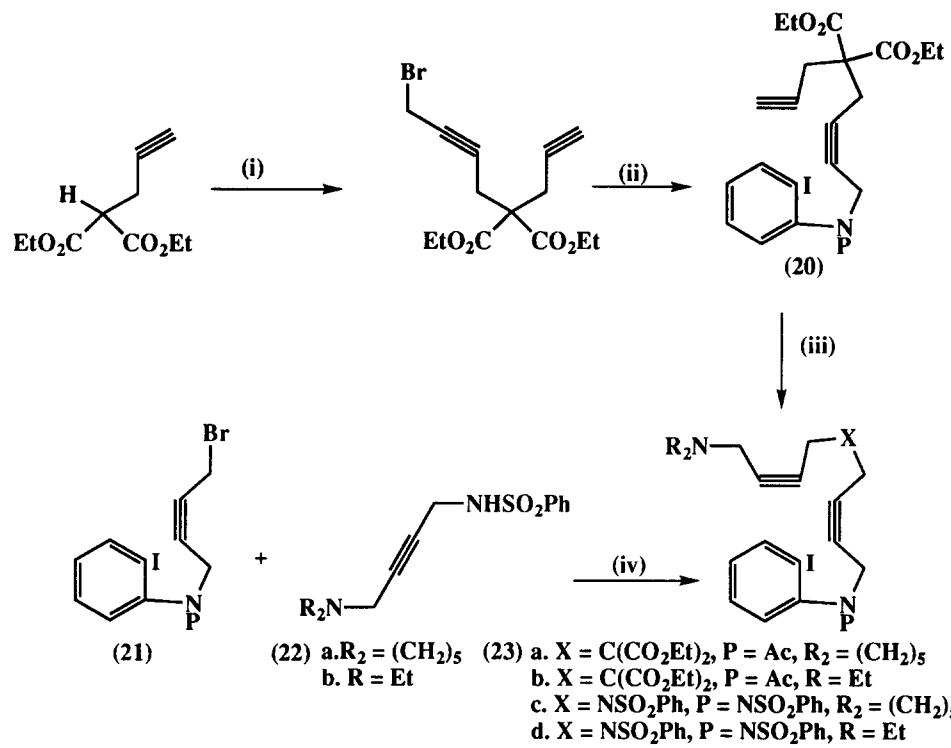
When (20) was subjected to palladium catalysed cyclisation-hydride capture employing catalyst A it underwent two sequential 5-exo-dig cyclisations to afford a 4.3:1 mixture (32%) of (24) and the indole (25).

The Mannich bases (23a-d) reacted with catalyst D with the addition of 1mol eq. of Ag_2CO_3 to give the tetracycles (27a-d) in good yield (Scheme 6) (Table 2).

Table 2 Cyclisation of (23a-d) to (27a-d)[a].

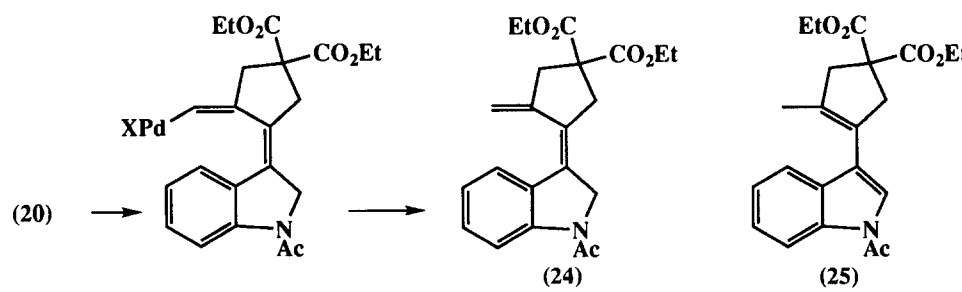
Mannich base	Product	X	P	R/R_2	Reaction Time(h)	Yield(%)
23a	27a	$C(CO_2Et)_2$	Ac	$(CH_2)_5$	1	77
23b	27b	$C(CO_2Et)_2$	Ac	Et	2	70
23c	27c	NSO_2Ph	NSO_2Ph	$(CH_2)_5$	2	60
23d	27d	NSO_2Ph	NSO_2Ph	Et	2	65
29	30	-	-	-	15	60

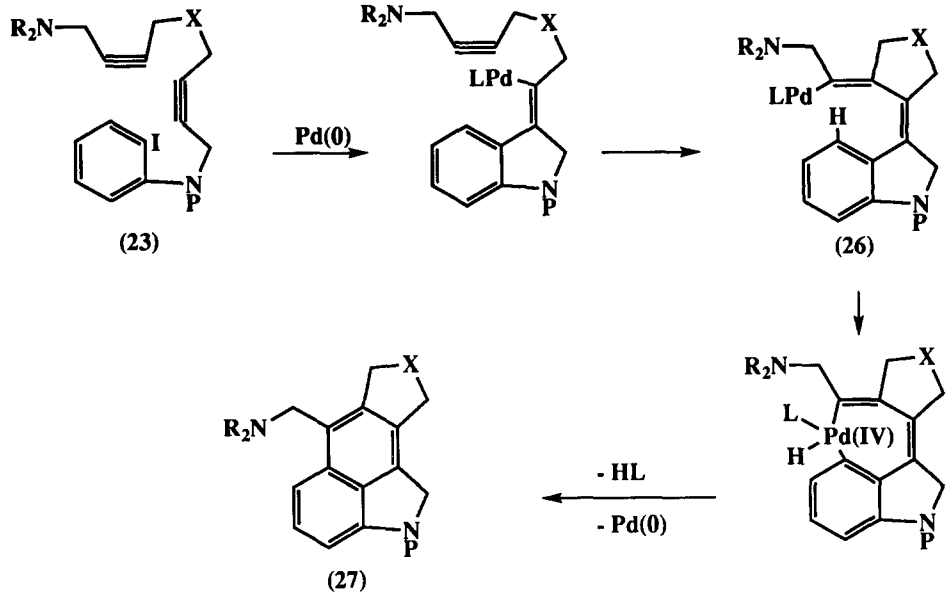
a. Reactions carried out at 80°C in MeCN employing catalyst D with the addition of 1mol. eq. of Ag_2CO_3.



Scheme 5 (i) NaOEt / EtOH, $BrCH_2C{\equiv}CCH_2Br$ (ii) 2 - iodoacetanilide / LDA/ toluene

(iii) HCHO / R_2NH / H_2O / H_2SO_4 / $CuSO_4$ (iv) NaH, THF, 25°C

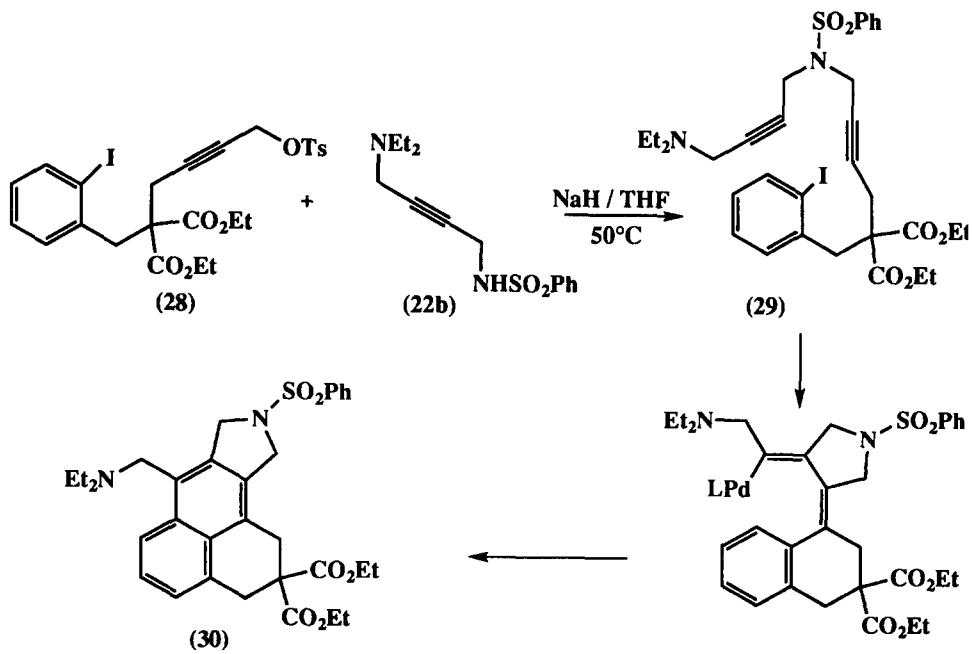




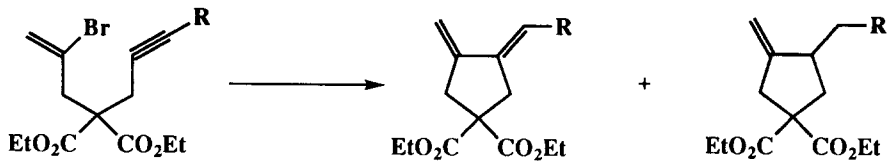
Scheme 6

Thus it was not possible to effect hydride capture in these cases. The close proximity of the vinylpalladium moiety to the peri-H in (26) together with the rigidity imparted by the 1,3-dienyl moiety promotes oxidative addition of the vinylpalladium(II) species to the peri-C-H bond leading, via a Pd(IV) intermediate,[19] to (27) (Scheme 6).

The related substrate (29) was prepared from (28) and (22b) and showed similar behaviour undergoing cyclisation using the same catalyst system to give (30) in good yield (Table 2).



B. Vinyl Halide Starter Species. Substrates (31a,b) were prepared by sequential alkylation of diethyl malonate first with the propargylic bromide and then with 2,3-dibromopropene.



(31) a. R = H
b. R = $SiMe_3$

(32) a. R = H
b. R = $SiMe_3$

(33)

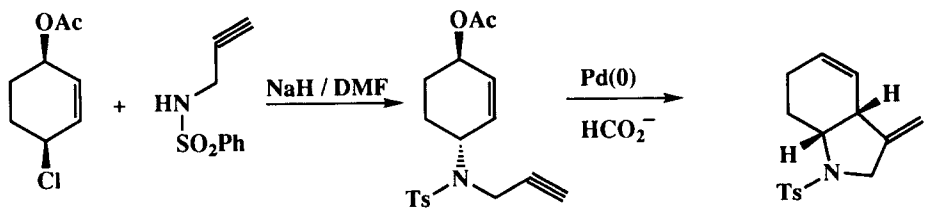
Cyclisation of (31a) over 43h at 30°C using catalyst C afforded (32a)(38%). At 80°C the reaction produced a 4.3:1 mixture (40%) of (32a) and (33a). The trimethylsilyl derivative (31b) cyclised under similar conditions, using benzene as solvent, to give (32b) (47%). Use of acetonitrile as solvent at 80°C together with variation of the amounts of piperidine and formic acid leads to increased yields of mixtures of products (Table 3).

Table 3 Cyclisation-hydride capture product distribution from (31b)[a].

Piperidine (mol equiv)	Formic acid (mol equiv)	Time(h)	Yield(%)[b]	Product ratio[c] (32a)	(32b)	(33b)
5.1	4.0	3	50[d]	1	1.5	-
7.6	6.0	9	66	1	2.9	-
12.0	6.0	12	80[e]	1.5	27	1
9.4	8.4	6	47[f]	-	1	-

a. All reactions were carried out at 80°C in MeCN using 5mol% $Pd(OAc)_2$ and 10mol% PPh_3.
b. Products isolated by preparative t.l.c.
c. Product ratio estimated from the 250 Mhz ^1H nmr spectra.
d. Large amount of unreacted starting material present.
e. Estimated by g.l.c.
f. Benzene used as solvent.

C. Allylic Acetate Starter Species. The seminal work of Oppolzer on metallo-ene reactions[20] augered well for the use of allylic acetate starter species. A suitable substrate (34) was prepared by alkylation of N-propargyl phenyl sulphonamide with 1-acetoxy-4-chlorocyclohex-2-ene.



(34) (35)

Allylic acetate (34) underwent cyclisation-hydride capture under the influence of catalyst C to afford (35)(50%).

Experimental. Melting points were determined on a Koffler hot-stage apparatus and are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 598 and 983 G instruments and refer to potassium bromide discs unless otherwise noted. Mass spectral data were obtained from VG 7070 and Autospec instruments operating at 70 eV. Nuclear magnetic resonance spectra were recorded on Bruker WM 250, QE 300 and Bruker AM 400 instruments operating at 250, 300 and 400 Mhz respectively. Unless otherwise specified deuteriochloroform was used as solvent. Microanalyses were obtained using a Carbo Erba MOD 11016 instrument. Preparative t.l.c. plates were prepared using silica gel 60 PF(Merck 7748). Column chromatography was performed with silica gel 60(Merck 9385). Petroleum ether refers to the fraction with b.p. 40-60°C.

Cyclisation Substrates

N-Propargyl-2-iodoacetanilide (5a). A saturated solution of 2-iodoacetanilide (7.83g, 0.03mol) in dry THF was added dropwise with stirring over 30 min to a solution of LDA (0.03mol) [prepared from $LiBu^n$ (18.8ml of 1.6M solution in hexane) and N,N-diisopropylamine (3.03g)] in dry THF (50ml) at -78°C. An 80% solution of propargyl bromide in dry toluene (4.45g, 0.03mol) was then added dropwise and the mixture allowed to come to room temperature with stirring overnight. After addition of saturated aqueous ammonium chloride solution (50ml) the mixture was extracted with ether (3x75ml), the ether extracts combined, dried ($MgSO_4$) and evaporated under reduced pressure. The residual oil was purified by column chromatography (SiO_2) eluting with 1:1 v/v ether-petroleum ether to afford the **product** (6.8g, 76%) as a pale yellow solid, m.p. 54-56°C (Found: C, 44.35; H, 3.4; N, 4.85. $C_{11}H_{10}INO$ requires C, 44.2; H, 3.35; N, 4.7%); δ7.96(dd,1H,ArH), 7.45 and 7.14(2xm, 2H and 1H, ArH), 5.10 and 3.78(2xdd, J17.4 and 2.5Hz, NCH_2), 2.22(t, J2.5Hz,≡CH) and 1.81(s, 3H,Me); m/z(%) 299(M^+,2), 257(11), 256(12), 173(14), 172(100), 130(35), 129(11), 103(12), 77(11) and 43(30); υ_{max}(nujol) 3250, 2100, 1640, 1570, 740 and 715cm^{-1}.

N-(But-2'-ynyl)-2-iodoacetanilide(5b). Prepared from 2-iodoacetanilide and but-2-ynyl bromide in an analogous manner to that described above. The **product** (62%) crystallised from ether-petroleum ether as colourless rods, m.p. 61-63°C (Found: C, 46.05; H, 3.8; N, 4.45; I, 40.75. $C_{12}H_{12}INO$ requires C, 46.05; H. 3.85; N, 4.45; I, 40.55%); δ7.95(dd, 1H, ArH), 7.44 and 7.13(2xm, 2H and 1H, ArH), 5.0 and 3.77(2xdq, 2H, J17.1 and 2.4Hz, NCH_2), 1.81(s, 3H, COMe) and 1.76(t, 3H, J2.4Hz, ≡ CMe); m/z(%) 313(M^+,14), 187(15), 186(100), 144(34), 143(21), 134(11), 115(15), 53(27) and 43(26); υ_{max}(nujol) 2000, 1650, 1520 and 740cm^{-1}.

N-(3'-Trimethylsilylprop-2'-ynyl)-2-iodoacetanilide (5c). Prepared from 2-iodoacetanilide and 3-trimethylsilylprop-2-ynyl bromide in an analogous manner to that described above. The **product** (60%) was obtained as a pale yellow thick oil (Found: C, 45.45; H, 4.35; H, 3.7. $C_{14}H_{18}INOSi$ requires C, 45.3; H, 4.9; N, 3.75%); δ7.95(d,1H, ArH), 7.42(m, 2H, ArH), 7.12(dt, 1H, ArH), 5.07 and 3.92(2xd, 2x1H, J17.6Hz, NCH_2), 1.82(s, 3H, Me) and 0.1(s, 9H, $SiMe_3$); m/z(%) 371(M^+,44), 356(13), 328(11), 245(21), 244(100), 83(24) and 73(55).

General procedure for the preparation of Mannich bases (5d-f). The secondary amine (1.2mol) was dissolved in water (80ml) and the solution was brought to pH9 by the addition of a solution of 50% sulphuric acid. Formalin solution (37%) (1.6mol) was added to the mixture followed by the acetylenic compound (5a)(1mol). A solution of cupric sulphate (5g) in water (50ml) was added, and the pH adjusted to 8.4 by the addition of excess amine. The reaction mixture was heated at 80°C with stirring until the greenish precipitate, formed at the initial stage, dissolved giving a yellow solution. The mixture was cooled, poured into cold concentrated ammonia (300ml), and the aqueous mixture extracted with dichloromethane (3x100ml). The

combined organic extracts were dried ($MgSO_4$) and evaporated. The residual oil was purified by flash column chromatography.

N-[4'-(1''-Piperidino)-but-2'-ynyl]-2-iodoacetanilide(5d). Prepared by the general method with heating at 80°C for 15min. The **product** (72%) was obtained as a colourless oil (Found: C, 51.75; H, 5.4; N, 7.25; I. 31.95. $C_{17}H_{21}N_2O$ requires C, 51.5; H, 5.4; N, 7.1; I, 32.0%); δ7.94 (d, 1H, ArH), 7.41(m, 2H, ArH), 7.11(m, 1H, ArH), 5.04 and 3.95(2xd, 2x1H, J17.3Hz, NCH_2), 3.18(s, 2H, NCH_2), 2.36 (br s, 4H, $2xCH_2$), 1.8(s, 3H, Me), 1.55(m, 4H, $2xCH_2$) and 1.31(m, 2H, CH_2); m/z(%) 397(M+1,4), 98(100), 85(17), 84(16), 71(6), 70(4), 57(9), 56(5) and 43(14).

N-(4'-Diethylaminobut-2'-ynyl)-2-iodoacetanilide(5e). Prepared by the general procedure with heating at 80°C for 2h. The **product** (58%) was obtained as a pale yellow oil (Found: C, 50.1; H, 5.55; N, 7.05; I,33.3. $C_{16}H_{21}IN_2O$ requires C, 50.0; H, 5.5; N, 7.3; I, 33.0%); δ7.94(d, 1H, ArH), 7.38(m, 2H, ArH), 7.11(m, 1H, ArH), 5.03 and 3.96(2xd, 2x1H, J16.3Hz, NCH_2), 3.34(s, 2H, NCH_2), 2.39(q, 4H, J7.2Hz, $\underline{CH_2}Me$), 1.08(s, 3H, COMe) and 0.99(t, 6H, $CH_2\underline{Me}$); m/z(%) 370(5), 369(28), 313(20), 312(100), 270(18), 244(32), 144(18), 143(63), 72(76) and 43(31); υ_{max}(film): 3020, 3000, 2900, 1700, 1465, 1150, 1050 and 775cm^{-1}.

N-[4'(1''-Pyrrolidino)-but-2'-ynyl]-2-iodoacetanilide(5f). Prepared by the general method with heating at 80°C for 15h. The **product** (63%) was obtained as a pale yellow thick oil (Found: C, 50.25; H, 5.0; N, 7.6; I, 32.95. $C_{16}H_{19}IN_2O$ requires C, 50.3; H, 5.0; N, 7.35; I, 33.2%); δ7.93(d; 1H, J7.9Hz, ArH), 7.41(m, 2H, ArH), 7.11(m, 1H, ArH), 5.04 and 3.91(2xd, 2x1H, J17.1Hz, NCH_2), 3.34(s, 2H, NCH_2), 2.47(br s, 4H, $2xNCH_2$), 1.79(s, 3H, COMe) and 1.74(br s, 4H, $2xCH_2$); m/z(%) 312(5), 261(3), 186(3), 134(4), 122(14), 108(7), 84(10), 70(100), 43(40) and 42(19).

N-(2-Iodobenzoyl)-N-methyl propargylamine (10a). A solution of 2-iodobenzoyl chloride (20.65g, 0.1mol) in dry methylene chloride (50ml) was added dropwise over 15min to a stirred solution of N-methylpropargylamine (13.89g, 0.2mol) in dry methylene chloride (50ml). The resulting mixture was stirred at room temperature for a further 2h, diluted with methylene chloride (100ml), washed with water, dried (anhy. Na_2SO_4) and the solvent removed. The residue was crystallised from hexane to afford the **product** (31.34g, 95%) as pale brown prisms, m.p. 47-49°C (Found: C, 44.25; H, 3.5; N, 4.7. $C_{11}H_{10}INO$ requires C, 44.15; H, 3.35; N, 4.7%); δ(amide rotational isomers) 7.8(m, 1H, ArH), 7.43-7.08(m, 3H, ArH), 4.6 and 3.9(2xd, NCH_2), 3.2 and 2.94(s, NMe), and 2.32(t, 1H, J2.3Hz, ≡CH).

N-(But-2-ynyl)-N-(2-iodobenzoyl)benzylamine(10b). (With Dr. B. Burns). a. A solution of but-2-ynyl tosylate (11.2g, 0.05mol) in dry acetontrile (30ml) was added dropwise to a well stirred solution of benzylamine (10.7g, 0.1mol), in dry acetonitrile (50ml). The resulting mixture was stirred for a further 3h at room temperature, filtered, the precipitate washed with acetonitrile (2x30ml) and the combined filtrates evaporated under reduced pressure. The residual oil was distilled to afford **N-but-2-ynyl-N-benzylamine** (5.64g, 71%), b.p. 80-84°C/0.025mmHg, as a colourless oil (Found: C, 83.0; H,7.75; N, 8.35. $C_{11}H_{13}N$ requires C, 82.95; H, 8.2; N, 8.8%); δ7.28(m, 5H, ArH), 3.83(s, 2H, NCH_2Ph), 3.35(s, 2H, ≡ CCH_2N), 1.83(s, 3H, Me) and 1.49(br s, 1H, NH); m/z(%) 159(M^+,20), 158(22), 144(19), 106(100), 91(67), 68(53) and 53(20), υ_{max}(film) 3315, 3025, 2915, 1601, 1492, 1098 and 780cm^{-1}.

b. A solution of 2-iodobenzoyl chloride (8.4g, 0.031mol) in dry benzene (15ml) was added dropwise with stirring over 15min to a solution of N-but-2-ynyl-N-benzylamine (5g, 0.031mol) and triethylamine (3.18g, 0.031mol) in dry benzene (40ml) and stirring was continued for a further 2h. The solvent was then removed under reduced pressure, the residue triturated with cold, dry ether to precipitate salts and filtered. Evaporation

of the filtrate and crystallisation of the residue from 40-60 petroleum ether-ether afforded the **product** (8.63g, 71%), m.p. 69-71°C, as colourless prisms (Found: C, 55.65; H, 4.3; N, 3.8. $C_{18}H_{16}INO$ requires C, 55.55; H, 4.15; N, 3.6%); δ(C_6D_6, 73°C) 7.45(m, 1H, ArH), 7.3(d, 1H, J7Hz, ArH), 7.1(m, 6H, ArH), 6.6(m, 1H, ArH), 4.4(s, 2H, NCH_2Ph), 3.6(s, 2H, ≡ CCH_2N) and 1.5(s, 3H, Me); m/z(%) 389(M^+,7), 336(21), 298(5), 262(20), 231(100), 203(51) and 91(90); υ_{max}(KBr) 3051, 2924, 1631 and 1594cm^{-1}.

N-[4'-(1''-Piperidinyl)but-2'-ynyl]-N-methyl-2-iodobenzamide(10c). Prepared by the general procedure for Mannich bases in 50% aqueous dioxan as solvent at 80°C for 2h. The **product** (73%) was obtained as a pale yellow oil. (Found: C, 51, 25; H, 5.35; N, 7.3; I, 31.75. $C_{17}H_{21}IN_2O$ requires C, 51.5; H, 5.35; N, 7.05; I, 32.0%); δ (amide rotational isomers) 7.82, 7.39, 7.24 and 7.08(4xm, 4x1H, ArH), 4.4 and 3.9(2xs, 2H, NCH_2), 3.27(d, 2H, 13.2Hz, NCH_2), 3.19 and 2.89(2xs, 3H, NMe), 2.48(m, 4H, 2xNCH_2), 1.60(m, 4H, 2xCH_2) and 1.42(br s, 2H, CH_2); m/z(%) 396(M^+,2), 318(25), 312(7), 244(22), 231(100), 135(30), 84(68) and 76(25).

N-[4'-(1''-Pyrrolidinyl)but-2'-ynyl]-N-methyl-2-iodobenzamide(10d). Prepared using the general procedure for Mannich bases. The **product** (60%) was obtained as a pale yellow oil (Found: C, 50.6; H, 5.15; N, 7.15; I, 33.1. $C_{16}H_{19}IN_2O$ requires C, 50.25; H, 5.0; N, 7.35; I, 32.2%); δ(amide rotational isomers) 7.82, 7.39, 7.25 and 7.08(4xm, 4x1H, ArH), 4.44 and 3.89(2xs, NCH_2), 3.41(m, 2H, NCH_2), 3.18 and 2.89(2xs, 3H, NMe), 2.60(m, 4H, NCH_2) and 1.8(br s, 4H, 2xCH_2); m/z(%) 312(M-C_4H_8N, 100), 231(56), 203(23), 186(12), 122(9), 105(36), 84(13), 77(33), 76(26) and 70(100).

N-[4'-Diethylaminobut-2'-ynyl)-N-methyl-2-iodobenzamide(10e). Prepared by the general procedure for Mannich bases. The product (71%) was obtained as a pale yellow oil (Found: C, 49.9; H, 5.5; N, 7.6; I, 33.4. $C_{16}H_2IN_2O$ requires C, 50.0; H, 5.5; N, 7.7; I, 33.0%); δ 7.82, 7.37, 7.19 and 7.08(4xm, 4x1H, ArH), 4.44 and 3.89(2xs, 2H, NCH_2), 3.19 and 2.89(2xs, 3H, NMe), 2.53(m, 4H, 2x$\underline{CH_2}$Me) and 1.10(m, 6H, 2x$CH_2\underline{Me}$); m/z(%) 385(M+1,4), 369(15), 313(17), 312(87), 244(28), 231(68), 203(21), 186(8), 146(9), 105(31), 86(90), 84(100), 77(25), 76(22) and 72(82).

N-[4'-(1''-piperidinyl)but-1,2-dienyl]-N-methyl-2-iodobenzamide[17, R_2=$(CH_2)_5$]. A mixture of alkyne (10c) (5mmol) and powdered NaOH (20mmol) in DMF (10ml) was stirred at room temperature for 4h. Water (50ml) was then added and the solution extracted with ether (2x50ml), the combined extracts dried (Na_2SO_4), filtered and the filtrate evaporated to afford the **product** as a colourless oil (90%) whose proton n.m.r. spectrum showed it to consist of a ca. 2.5:1 mixture of (17a) and (17b). This was used directly for the Diels-Alder reaction. δ7.85(m, 1H, ArH), 7.65(d, 1H, H_A), 7.4(t, 1H, Ar), 7.25 and 7.2(2xm, 2x1H, ArH), 6.4(d, 1H, H_A), 5.95 and 5.8(d + br s, 1H, H_B), 3.2 and 2.85(2xs, 3H, NMe), 3.1-3.2(s+m overlapping with NMe, 2H, NCH_2), 2.5(br s, 4H, 2 x ring NCH_2), 1.6(br s, 4H, 2 x CH_2) and 1.45(br s, 2H, CH_2).

2-Iodobenzyl pent-3-ynyl ether(18). Sodium hydride (0.5g, 50% dispersion in mineral oil, 0.02mmol) was added portionwise to a stirred solution of pent-3-yn-1-ol(0.84g, 0.01mmol) in dry DMF(20ml) at room temperature and the mixture stirred for 1h. A solution of 2-iodobenzyl chloride (2.5g, 0.01 mmol) in dry DMF (10ml) was then added dropwise with stirring and a resultant mixture stirred overnight. Water (100ml) was then added and the mixture extracted with Et_2O (2 x 100ml). The combined ether extracts were dried (Na_2SO_4), filtered and the filtrate evaporated under reduced pressure. The residue was distilled to afford the **product** (2.1g, 70%) as a colourless oil, b.p. 130-135°C/0.5mmHg (Found: C, 48.5; H, 4.55. $C_{12}H_{13}IO$ requires C, 48.0; H, 4.55%); δ7.8(d, 1H, J7.9Hz, ArH), 7.44(d, 1H, J7.8Hz, ArH), 7.25 and 7.0(2xt, 2x1H, ArH), 4.5(s, 2H, $ArCH_2O$), 3.6(t, 2H, CH_2O), 2.5(br s, 2H, CH_2) and 1.8(s, 3H, Me); m/z(%) 300(M^+,2), 299(3), 285(57), 217(100), 128(15), 91(51), 69(10) and 42(18).

N-(5',5'-Diethoxycarbonylocta-2',7'-diynyl)-2-iodoacetanilide(20). a. Diethyl propargylmalonate (9.9g, 0.05mmol) was slowly added to an ethanolic solution of sodium ethoxide (25ml) (prepared from Na 1.15g). The resulting mixture was stirred at room temperature for 15 min. 1,4-Dibromobut-2-yne (12.7g, 0.06mmol) was then added dropwise and stirring continued for a further 16h when water (25ml) was added and the resulting mixture was extracted with ether (3x40ml). The combined ether extracts were washed with brine, dried ($MgSO_4$), filtered and evaporated. The residual oil was distilled to afford **diethyl 4-bromobut-2-ynyl propargylmalonate** (6.4g, 39%), b.p. 150-155°C/0.05mmHg as a pale yellow oil (Found: C, 51.0; H, 5.2; Br, 24.15. $C_{14}H_{17}BrO_4$ requires C, 51.1; H, 5.2; Br, 24.25%); δ 4.23(m, 4H, 2xOCH_2), 3.86(t, 2H, J2.1Hz, CH_2Br), 2.92(m, 4H, 2xCH_2), 2.03(t, 1H, J2.1Hz, ≡ CH) and 1.28(m, 6H, $CH_2\underline{Me}$); m/z(%) 331/329 (M^+,2), 249(100), 175(44), 147(23) and 103(24).

b. 2-Iodoacetanilide (0.006mmol) and diethyl 4-bromobut-2-ynyl propargylmalonate (0.006mmol) were reacted according to the procedure used for the preparation of N-propargyl-2-iodoacetanilide (5a). After purification by flash chromatography eluting with 7:3 v/v ether-petroleum ether the **product** (70%) was obtained as a pale yellow thick oil (Found: C, 51.55; H, 4.85; N, 2.95; I, 24.6. $C_{22}H_{24}INO_5$ requires C, 51.9; H, 4.75; N, 2.75; I, 24.9%); δ7.95(dd, 1H, J7.9 and 1.1Hz, ArH), 7.5-7.42(m, 2H, ArH), 7.15(dt, 1H, J7.7 and 1.9Hz, ArH), 5.05 and 3.76(2xd, 2x1H, J17.2Hz, NCH_2) 4.19(q, 4H, J7.1Hz, $\underline{CH_2}Me$), 3.0 and 2.85(2xs, 2x2H, 2xCH_2), 2.05(t, 1H, J2.6Hz, ≡ CH), 1.80(s, 3H, COMe) and 1.27(t, 6H, J7.1Hz, $CH_2\underline{Me}$); m/z(%) 509(M^+,44), 464(19), 382(39), 336(12), 312(26), 244(100), 91(33) and 43(37).

N-[9'-(1''-Piperidinyl)nona-2'7'-diynyl)]-2-iodoacetanilide(23a). A 4.0mmol run based on compound (20) using the general procedure for Mannich bases afforded the **product** (52%) as a colourless thick oil after column chromatography eluting with 7:3 v/v ether-petroleum ether. (Found: C, 55.25; H, 6.0; N, 4.85;I, 20.9. $C_{28}H_{35}IN_2O_5$ requires C, 55.45; H, 5.8; N, 4.6; I, 20.95%); δ7.88(d, 1H, J7.6Hz, ArH), 7.38(m, 2H, ArH), 7.06(m, 1H, ArH), 4.98 and 3.69(2xd, 2x1H, J17.2Hz, NCH_2), 4.12(q, 4H, J6.6Hz, 2xOCH_2), 3.16(s, 2H, NCH_2), 2.87 and 2.79(2xs, 2x2H, 2xCH_2), 2.32(br s, 4H, 2xNCH_2), 1.73(s, 3H, COMe), 1.54(m, 4H, 2xCH_2), 1.31(m, 2H, CH_2) and 1.17(t, 6H, J6.6Hz, 2xMe); m/z(%) 606(M^+,7), 561(23), 521(13), 479(7), 448(7), 348(31), 332(77), 272(44), 244(100), 189(18), 137(80), 84(43), 77(25) and 43(85).

N-(9'-Diethylaminonona-2',7'-diynyl)-2-iodoacetanilide(23b). Prepared in an analogous manner to the foregoing compound except that chromatography employed ether as eluant. The **product** (65%) was obtained as a thick colourless oil (Found: N, 4.8. $C_{27}H_{35}IN_2O_5$ requires N, 4.7%); HRMS 594.1596, $C_{27}H_{35}IN_2O_5$ requires 594.1590; δ 7.94(d, 1H, J8.0Hz, ArH), 7.42(m, 2H, ArH), 7.13(t, 1H, J8.0Hz, ArH), 4.17(q, 4H, J7.0Hz, 2xOCH_2), 5.04 and 3.75(2xd, 2x1H, J17.2Hz, NCH_2), 3.37, 2.92 and 2.84(3xs, 3x2H, 3xCH_2), 2.47(q, 4H, J7.0Hz, 2xNCH_2), 1.79(s, 3H, COMe), 1.22(t, 6H, J7.0Hz, 2xMe) and 1.04(t, 6H, J7.0Hz, 2xMe); m/z(%) 594(M^+,8), 551(5), 521(20), 467(6), 396(4), 334(83), 320(71), 260(37), 188(13), 125(60), 110(20), 86(42), 77(25), 72(41), 58(37) and 43(100).

N-(4'-Bromobut-2'-ynyl)-N-phenylsulphonyl-2-iodoaniline(21). A solution of N-phenylsulphonyl-2-iodoaniline (3.6g, 10mmol) in DMF (10ml) was added dropwise to a cooled (ice - salt bath) stirred solution of NaH (60% dispersion in mineral oil) (0.48g, 20mmol) in dry DMF (20ml) and stirring was continued for 30 min. 1,4-Dibromobut-2-yne(2.33g, 10mmol) was then added dropwise and the resulting mixture was heated at 60°C for 15h. After cooling the solvent was removed under reduced pressure, the residue taken up in dichloromethane (3x30ml). The dichloromethane solution was washed with water (50ml); dried ($MgSO_4$), filtered and evaporated to give a brown thick oil which was purified by flash column chromatography eluting

with 2:3 v/v ethyl acetate - petroleum ether to give the **product** (2.0g, 40%) as a pale yellow gum. HRMS: 491.893/489.898. $C_{16}H_{13}BrINO_2S$ requires 491.895/489.897. δ 7.93 - 7.07(m, 9H, ArH), 4.86 and 4.15(2xd, 2x1H, J18.4Hz, NCH_2) and 3.73(s, 2H, CH_2), m/z(%) 492/490(M^+,3), 410(8), 359(22), 283(100), 142(93), 77(82) and 76(29).

Mannich Base (23c). a. N-Phenylsulphonyl propargylamine was reacted with formalin and piperidine according to the general procedure for Mannich bases. Work up followed by column chromatography eluting with 7:3 v/v ether-methanol afforded **N-phenylsulphonyl-4-(1'-piperidinyl)but-2-ynlamine (22a)** (50%) as a pale yellow thick oil. δ 7.91 - 7.48(m, 5H, ArH), 3.87(s, 2H, CH_2), 3.0(s, 2H, CH_2), 2.26(m, 4H, 2xCH_2), 1.55(m, 4H, 2xCH_2) and 1.41(m, 2H, CH_2); m/z(%) 292(M^+,4), 135(17), 122(49), 98(47), 84(35) and 77(100).

b. A solution of N-phenylsulphonyl-4-(1'-piperidinyl)propargylamine (22a) (3.37, 11.5mmol) in freshly distilled THF(20ml) was added dropwise to a stirred solution of sodium hydride (60% dispersion in mineral oil) (0.55g, 22.9mmol) and stirring was continued for further 15 min. A solution of compound (19) (5.65g, 11.5mmol) in freshly distilled THF (25ml) was then added dropwise and the resulting mixture was stirred at room temperature for 15h. The solvent was then evaporated under reduced pressure, the residue extracted into dichloromethane (3x50ml) and the combined extracts washed with water, dried ($MgSO_4$) and the solvent evaporated. The residue was purified by flash column chromatography eluting with 19:1 v/v ether-methanol to afford the **product** (3.8g, 47%) as pale yellow gum. HRMS: 701.0876. $C_{31}H_{32}IN_3O_4S_2$ requires 701.0879. δ 7.92-7.03(m, 14H, ArH), 4.58(d, 1H, J17.5Hz, NCH), 4.02 and 3.94(2xs, 2x2H, 2xNCH_2), 3.03(m, 3H, 3xNCH), 2.26(m, 4H, 2xCH_2), 1.55(m, 4H, 2xCH_2) and 1.40(m, 2H, CH_2); m/z(%) 702(M+1,5), 560(20), 419(3), 335(7), 84(37) and 77(100).

Mannich Base (23d). a. N-Phenylsulphonyl propargylamine was reacted with formalin and diethylamine according to the general procedure. Work up followed by column chromatography eluting with 7:3 v/v ether-methanol afforded **N-phenylsulphonyl-4-diethylaminobut-2-ynylamine (22b)** (40%) as a pale yellow solid, m.p. 102-103°C (Found: C, 59.85; H, 7.3; N, 9.85; S, 11.35. $C_{14}H_{20}N_2SO_2$ requires C, 60.0; H, 7.2; N, 10.0; S, 11.4%); δ 7.99-7.5(m, 5H, ArH), 3.8(s, 2H, NCH_2), 3.11(s, 2H, NCH_2), 2.29(q, 4H, J7.0Hz, 2xNCH_2) and 0.9(t, 6H, J6.9Hz, 2xMe); m/z(%) 280(M^+,5), 265(100), 222(9), 170(17), 124(6), 110(32), 77(69), 72(6) and 58(21).

b. N-Phenylsulphonyl-4-diethylaminobut-2-ynylamine (22b) and (21) were reacted as described above. Work up followed by column chromatography eluting with 7:3 v/v ether-methanol gave the **product** (52%) as a pale yellow thick oil. HRMS: 689.0826. $C_{30}H_{32}IN_3O_4S_2$ requires 689.0834. δ 7.91-7.03(m, 14H, ArH), 4.58(d, 1H, J17.8Hz, NCH), 3.94(m, 5H, NCH), 3.23(s, 2H, NCH_2), 2.35(q, 4H, J7.1Hz, 2xCH_2) and 0.98(t, 6H, J7.0Hz, 2xMe); m/z(%) : 690(M^++1,10), 548(3), 78(57), 74(70) and 58(100).

Mannich Base (29). a. A solution of diethyl 2-iodobenzylmalonate (3.7g, 0.01mol) in dry THF(20ml) was added dropwise to a stirred solution of sodium hydride (60% dispersion in mineral oil) (0.48g, 0.02mol) in freshly distilled dry THF(50ml) and stirring was continued for a further 30 min. A solution of 1,4-butyne diol ditosylate (4.92g, 0.012mol) in dry THF(50ml) was then added and the mixture boiled under reflux for 15h. The solvent was then removed under reduced pressure and the residue extracted with dichloromethane (3x50ml). The combined extracts were washed with water, dried ($MgSO_4$), filtered and the solvent removed. The residue was purified by column chromatography eluting with 2:3 v/v ether-petroleum ether to give **28** (3.2g, 55%) as a thick colourless oil. (Found: C, 50.35; H, 4.65;I, 21.2. $C_{25}H_{27}IO_7S$ requires C, 50.2; H, 4.55; I, 21.2%); δ 7.83-6.88(m, 8H, ArH), 4.69(s, 2H, CH_2), 4.18(m, 4H, 2xOCH_2), 3.47 and 2.73(2xs, 2x2H,

2xCH_2), 2.41(s, 3H, Me) and 1.21(m, 6H, 2xMe); m/z(%) 471(3), 427(4), 325(5), 169(14), 155(34), 91(100) and 77(17).

b. A solution of N-phenylsulphonyl-4-diethylaminobut-2-ynylamine (0.86g, 3.0mmol) in dry THF(10ml) was added dropwise to a stirred solution of sodium hydride (60% disperion in mineral oil) (0.15g, 6.0mmol) in freshly distilled dry THF(20ml) and stirring continued for 30 min. A solution of (26) in dry THF (20ml) was then added and the mixture heated at 50°C for 15h. The solvent was then evaporated under reduced pressure and the residue extracted with dichloromethane (3x40ml). The combined organic extracts were washed with water, dried ($MgSO_4$), filtered and the filtrate evaporated. The residue was purified by column chromatography eluting with 4:1 v/v ether-methanol to give the **product** (1.2g, 55%) as a pale yellow gum. HRMS: 706.1570. $C_{32}H_{39}IN_2O_6S$ requires 706.1574. δ 7.76 - 6.82(m,9H, ArH), 4.09(m, 8H), 3.4, 3.16 and 2.62(3xs, 3x2H, 3xCH_2), 2.27(q, 4H, J6.9Hz, 2xCH_2), 1.14(t,6H, J6.9Hz, 2xMe) and 0.89(t, 6H, J7.0Hz, 2xMe); m/z(%) 707(M^++1, 41), 691(57), 677(9), 661(14), 633(11), 579(5), 565(63), 123(69), 77(100), 72(33) and 58(52).

Diethyl 2-bromoprop-2-enyl-(3'-trimethylsilylprop-2'-ynyl)malonate(31b). BuLi (6.3ml of a 1.6M solution in hexane, 0.01mol) was added to a solution of diethyl (2-bromoprop-2-enyl) propargyl malonate (3.17g, 0.01mol) in dry THF(50ml) stirred and cooled to - 63°C. The mixture was stirred for 15 min. and then trimethylchlorosilane (1.09g, 0.01ml) was added. The mixture was allowed to warm to room temperature with stirring overnight. The solvent was removed under reduced pressure and the residue partitioned between water and ether. The ether extract was dried ($MgSO_4$), filtered and the filtrate evaporated. The residual oil was distilled to afford the **product** (2.18g, 54%) as a colourless oil, b.p. 120-122°C/0.01mmHg (Found: C, 49.85, H, 6.9. $C_{16}H_{25}BrO_4Si$ requires C, 49.35; H, 6.45%); δ5.69 and 4.48(2xd, 2x1H, = CH_2), 4.09(m,4H, $\underline{CH_2}$Me), 3.15 and 2.80(2xs, 2x2H, 2xCH_2) and 1.14(t,6H, $CH_2\underline{Me}$); m/z(%) 390/388(M^+,1), 309(89), 236(9), 235(33), 207(34) and 73(100); ν_{max}(film) 2960, 2945, 2885, 2170, 1725, 1615, 1418, 1280, 1245, 1180, 1025, 840, 768, 695 and 648cm^{-1}

***trans* 1-Acetoxy-4-(N-p-toluenesulphonyl-N-prop-2-ynyl)aminocyclohex-2-ene(34).** Sodium hydride (0.5g, 60% dispersion in mineral oil) was added portionwise to a stirred solution of N-(p-toluenesulphonyl)propargylamine (2.09g, 0.01mol) in dry THF(30ml) at room temperature and the resulting mixture stirred for a further 1h. A solution of cis 1-acetoxy-4-chlorocyclohex-2-ene(1.76g, 0.0lmol)[21] in DMF(20ml) was added dropwise with stirring and the mixture then stirred and heated at 78°C for 2h. Work up in the usual way afforded the **product** (2.2g, 63%) which crystallised from ether-petroleum ether as colourless prisms, m.p. 110-111°C (Found: C, 62.5; H, 5.95; N, 4.1. $C_{19}H_{21}NO_4S$ requires C, 62.25; H, 6.05; N, 4.05%); δ 7.78 and 7.30(2xd, 2x2H, J6.7Hz, ArH), 5.79(dt, 1H, J1.9 and 10.2Hz, = CH), 5.48(d, 1H, J10.2Hz, = CH), 5.38(m, 1H, CHN), 4.6(m, 1H, CHOAc), 4.1 and 3.85(2xdd, 2x1H, J2.4 and 18.5Hz, NCH_2), 2.4 and 2.0(2xs, 2x3H, ArMe, COMe) and 2.2 - 1.6(m, 4H, 2xCH_2); m/z(%) 347(M^+,0.5), 290(3), 289(11), 288(53), 287(43), 283(8), 192(18), 150(23), 139(28), 132(64), 122(56), 91(94) and 43(100).

General Procedure for Palladium Catalysed Cyclisation-Hydride Capture.

Catalyst A: A mixture of the iodo- or bromo-substrate(2mmol), palladium acetate (0.2mmol), triphenylphosphine (0.4mmol), tetraethylammonium chloride (2mmol), formic acid (6mmol) and piperidine (8mmol) in MeCN(50ml) was stirred and heated at 60°C under a nitrogen atmosphere until t.l.c. 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 t.l.c. as appropriate afforded the product.

Catalyst B: The procedure was as for catalyst A but with sodium formate (1.1mol equiv.) replacing formic acid and piperidine.

Catalyst C: The procedure is identical to that for catalyst A but without tetraethylammonium chloride.

Catalyst D: The procedure is identical to that used for catalyst B but without tetraethylammonium chloride.

N-Acetyl-3-ethylidene indoline(6a). Prepared using a modified catalyst C with 1mol equiv. Ag_2CO_3 but without piperidine and a reaction time of 16h at room temperature. The product (60%) was a thick yellow oil. HRMS: 187.0998. $C_{12}H_{13}NO$ requires 187.0997. δ 8.28(d, 1H, ArH), 7.41 - 7.0(m, 3H, ArH), 6.0(m, 1H, = CH), 4.53(t, 2H, J2.7Hz, NCH_2), 2.22(s, 3H, COMe) and 1.77(dt, 3H, J5.1 and 1.9Hz); m/z(%) 187(M^+,55), 145(19), 144(41), 130(100), 118(3), 117(7) and 43(13).

N-Acetyl-3-trimethylsilylmethylidine indoline(6b). Prepared using catalyst A at 60°C with a 1h reaction time. Work up followed by preparative t.l.c. eluting with 2:3 v/v ether-petroleum ether afforded the **product** (50%) as a colourless solid, m.p. 78-80°C (Found: C, 68.2; H, 7.55; N, 5.95. $C_{14}H_{19}NOSi$ requires C, 68.5; H, 7.8; N, 5.7%); δ8.29 and 7.43(2xd, 2x1H, J8.2 and 7.5Hz, ArH), 7.25(dt, 1H, J7.8 and 1.2Hz, ArH), 7.03(dt, 1H, J7.5 and J7.5 and 0.9Hz, ArH), 6.0(t, 1H, J2.7Hz, ≡ CH), 4.62(d, 2H, J2.8Hz, NCH_2) and 2.33 and 0.19(2xs, 3H and 9H, COMe and $SiMe_3$); m/z(%) 245(M^+,64), 230(18), 202(13), 130(100), 73(31) and 43(13).

N-Acetyl-3-(1'-piperidinyl)methylidine indoline(6c). Prepared over 5h at 60°C using catalyst D together with Ag_2CO_3 (1mol equiv.). Work up and purification by preparative t.l.c. eluting with 1:1 v/v ether-methanol afforded the product (54%) as a pale yellow solid, m.p. 65°C. HRMS: 270.1725. $C_{17}H_{22}N_2O$ requires 270.1732. δ8.27(d, 1H, J7.8Hz, ArH), 7.41(d, 1H, J7.6Hz, ArH), 7.23 and 7.03 (2xt, 2x1H, J7.6Hz, ArH), 6.03(m, 1H, = CH), 4.62(s, 2H, NCH_2), 3.05(d, 2H, J7.0Hz, NCH_2), 2.46(m, 2x2H, 2xCH_2), 2.25(s, 3H, COMe), 1.62(m, 4H, 2xCH_2) and 1.5(m, 2H, CH_2); m/z(%) 186(6,M-NC_5H_{10}), 185(44), 144(34), 143(100), 115(13), 84(11) and 43(25).

N-Acetyl-3-diethylaminomethylidine indoline(6d). Prepared and worked up in an analogous manner to that described for (6c) but with a reaction time of 15h. The **product** (56%) was obtained as a pale yellow solid, m.p. 49-50°C. HRMS: 258.1730. $C_{16}H_{22}N_2O$ requires 258.1732. δ8.29(d, 1H, J8.0Hz, ArH), 7.43(d, 1H, J7.5Hz, ArH), 7.24(m, 1H, ArH), 7.05(t, 1H, J7.4Hz, ArH), 6.04(m, 1H,=CH), 4.63(s, 2H, NCH_2), 3.18(d, 1H, J6.4Hz, NCH_2), 2.59(q, 4H, J6.9Hz, $\underline{CH_2}Me$), 2.27(s, 3H, COMe) and 1.08(t, 6H, J6.9Hz, $CH_2\underline{Me}$); m/z(%) 258(M^+,10), 229(12), 186(25), 185(73), 144(78), 143(100), 130(18), 86(42) and 43(27).

General Procedure for Sequential Cyclisation-Diels-Alder Cycloaddition. A mixture of Mannich base (1mmol), palladium acetate (0.1mmol), triphenylphosphine (0.2mmol), sodium formate (1.5mmol) and thallium carbonate (1mmol) was stirred in boiling acetonitrile (25ml) under reflux until the reaction was complete (t.l.c. monitoring). N-Methylmaleimide (1.1mmol) was then added and stirring and heating was continued for a further hour. The solvent was then evaporated and the residue extracted into chloroform (3x25ml) and washed with water (50ml). The combined organic layers were dried ($MgSO_4$) and concentrated and the residue purified by column chromatography or preparative t.l.c. to give the appropriate Diels-Alder adduct.

Diels-Alder Adduct (9a). The product (56%) was obtained after a 3h cyclisation phase followed by 1h for the Diels-Alder reaction. Purification by preparative t.l.c. eluting with ethyl acetate afforded a colourless solid which crystallised as colourless prisms from ether, m.p. 144-146°C (Found: C, 68.75; H, 6.85; N, 11.25. $C_{21}H_{25}N_3O_3$ requires C, 68.65; H, 6.85; N, 11.45%); δ7.46(d, 1H, J7.5Hz, ArH), 7.31(m, 2H, ArH), 7.06(m, 1H,

ArH), 6.27(m, 1H,=CH), 4.93(m, 1H, H_d), 4.33(t, 1H, J7.3Hz, H_a), 3.53(m, 2H, H_b and H_c), 2.98(m, 4H, 2xCH_2), 2.74(s, 3H, NMe), 2.60(s, 3H, COMe) and 1.15(t, 6H, J6.9Hz, 2xMe); m/z(%) 256(100, M-N-methylmaleimide), 214(51), 213(67), 195(9), 184(6), 168(12), 141(5), 111(25) and 43(35).

n.O.e. data for (9b).

Proton	%Enhancement		
irradiated	H_a	H_d	$H_b + H_c$
H_a	-	11.4	9.2
H_d	10.1	-	12.1
$H_b + H_c$	14.9	17.7	-

Diels-Alder Adduct(9b). After a 2h reaction time and work up the product (60%) was obtained as a pale yellow solid after purification by preparative t.l.c. eluting with ethyl acetate. It crystallised as colourless prisms from ether-ethyl acetates, m.p. 155-157°C. HRMS: 365.1731. $C_{21}H_{23}N_3O_3$ requires 365.1739. δ7.43(d, 1H, J7.5Hz, ArH), 7.32(m, 2H, ArH), 7.04(m, 1H, ArH), 6.24(m, 1H,=CH), 4.98(m, 1H, H_a), 4.32(t, 1H, J7.1Hz, H_b), 3.42(t, 1H, J6.7Hz, H_c), 2.98(m, 2H, 2xNCH), 2.88(m, 1H, H_d), 2.77(m, 2H, 2xNCH), 2.72(s, 3H, NMe), 2.60(s, 3H, COMe), and 1.93(m, 4H, 2xCH_2); m/z(%) 365(M^+,3), 255(37), 254(100), 212(91), 211(95), 184(9), 169(29), 142(13), 141(12), 111(52), 77(8), 70(12) and 43(53).

n.O.e. data for (9c).

Proton	%Enhancement			
irradiated	H_a	H_b	H_c	H_d
H_a	-	11.3	-	10.9
H_b	11.7	-	10.6	
H_c	-	14.2	-	9.8

N-Methyl-1,2,3,4-tetrahydro-4-methylidine isoquinolin-1-one(12a). Prepared using catalyst A and a reaction time of 2h. Work up followed by preparative t.l.c. eluting with 1:1 v/v ether-petroleum ether afforded the **product** (60%) as a colourless oil. HRMS: 173.0834. $C_{11}H_{11}NO$ requires 173.0840. δ8.16(d, 1H, J7.9Hz, ArH), 7.51(m, 3H, ArH), 5.6 and 5.17(2xs, 2x1H,=CH_2), 4.16(s, 2H, NCH_2) and 3.1(s, 3H, NMe); m/z(%) 173(M^+,100), 172(30), 158(5), 144(27), 138(8), 104(6) and 76(6); ν_{max}(film) 3059, 2951, 2922, 2850, 1642, 1597, 1491 and 775cm^{-1}.

N-Benzyl-1,2,3,4-tetrahydro-4-ethylidine isoquinolin-1-one(12b). (With Dr. B. Burns). Prepared using catalyst A at 60°C for 8h. Work up followed by preparative t.l.c. eluting with 1:1 v/v ether-petroleum ether afforded the **product** (50%) as a pale yellow oil. HRMS: 263.1310. $C_{18}H_{17}NO$ requires 263.1310. δ8.19(d, 1H, J7.9Hz, ArH), 7.37(m, 8H, ArH), 6.15(q, 1H, J6.8Hz,=CH), 4.85(s, 2H, $PhCH_2$), 4.14(s, 2H, NCH_2) and 1.69(d, 3H, J6.8Hz, Me); m/z(%) 263(M^+,57), 262(7), 248(23), 172(32), 159(29) and 91(100); ν_{max}(film) 3051, 2923, 1632 and 1594cm^{-1}.

N-Methyl-1,2,3,4-tetrahydro-4-(1'-piperidinylamino)ethylidine isoquinolin-1-one(12c). Prepared over 12h at 60°C using catalyst D with the addition of $TlNO_3$ (1mol. equiv.). Work up followed by preparative t.l.c. eluting with 1:1 v/v ether-methanol afforded the **product** (53%) as a pale yellow solid, m.p. 68-69°C (Found: C, 75.35; H, 8.05; N, 10.15. $C_{17}H_{22}N_2O$ requires C, 75.5; H, 8.2; N,10.35%); δ8.07 and 7.49(2xd, 2x1H,

J7.5Hz, ArH), 7.39 and 7.31(2xt, 2x1H, J7.5Hz, ArH), 6.15(m, 1H, = CH), 4.19(s, 2H, NCH_2), 3.1(s, 3H, NMe), 3.06(d, 2H, J6.9Hz, = $CH\underline{CH_2}$), 2.39(br s, 4H, $2xCH_2$), 1.55(m, 4H, $2xCH_2$) and 1.40(m, 2H, CH_2); n.O.e. (%): irradiation of H_A effected enhancement of the signal for H_B (17.5%) m/z(%) 270(M^+,3), 187(4), 186(31), 185(100), 157(6) and 84(6).

N-Methyl-3-vinylisoquinolin-1-one(13). Prepared over 12h at 60°C using catalyst A but without addition of piperidine. Work up followed by preparative t.l.c. eluting with 1:1 v/v ether-petroleum ether afforded the **product** (32%) as an off white solid, m.p. 52°C. HRMS: 185.0843. $C_{12}H_{11}NO$ requires 185.0840. δ8.47(d, 1H, J8.0Hz, ArH), 7.69(m, 2H, ArH), 7.52(m, 1H, ArH), 7.21(s, 1H,=CHN), 6.92(m, 1H, $\underline{CH}=CH_2$), 5.56(d, 1H, J17.2Hz, CH=C<u>H</u>H), 5.32(d, 1H, J11.0Hz, CH=CH<u>H</u>) and 3.64(s, 2H, NMe); m/z(%) 185(M^+,17), 184(100) 157(13), 156(17), 142(12), 128(14), 116(21), 115(46) and 77(7).

Diels-Alder Adduct(14). Diene (13) (1mmol) and N-methylmaleimide (1.1mmol) were reacted over 2h according to the general procedure. Work up afforded the **product** (80%) as an off white solid, m.p. 108-110°C (Found: C, 68.75; H, 5.55; N, 9.3. $C_{17}H_{16}N_2O_3$ requires C, 68.9; H, 5.45; N, 9.45%); δ8.26 and 7.6(2xd, 2x1H, ArH), 7.4(m, 2H, ArH), 6.5(m, 1H, = CH), 4.38(m, 1H, NCH), 3.66(m, 2H), 3.3(s, 3H, NMe), 3.24-3.0(m, 2H) and 2.78(s, 3H, NMe); m/z(%) 296(M^+,19), 295(2), 294(9), 292(5), 263(5), 231(2), 209(8), 186(13), 185(100) and 184(14).

Diels-Alder Adduct(16a). a. Prepared by the general procedure from (10c) with a cyclisation reaction time of 12h. Preparative t.l.c. eluting with 7:3 v/v ether-methanol afforded the **product** (70%) as a pale yellow solid which crystallised from chloroform as colourless prisms, m.p. 162°C (Found: C, 67.45; H, 6.45; N, 10.75. $C_{22}H_{25}N_3O_3$. 0.12 $CHCl_3$ requires C, 67.45; H, 6.45; N, 10.65%); δ8.24(dd, 1H, J7.6 and 1.4Hz, ArH), 7.59(d, 1H, J7.6Hz, ArH), 7.4(m, 2H, ArH), 6.66(m, 1H, = CH), 4.49(br s, 1H, NCH), 3.64(m, 2H, CHCO), 3.33(s, 3H, NMe), 2.97(m, 3H, 3xNCH), 2.73(s, 3H, NMe), 2.60(m, 2H, 2xNCH) and 1.83-1.53(m, 6H, $3xCH_2$); m/z(%) 268(100), 184(20), 111(49), 84(16) and 77(16).

b. Prepared from the preformed allene [17, R_2 = $(CH_2)_5$] and N-methylmaleimide in boiling acetonitrile over 1h. The **product** (80%) was identical to that described above.

Diels-Alder Adduct(16b). Prepared by the general method with a cyclisation time of 6h. Purification by preparative t.l.c. eluting with 7:3 v/v ether-methanol afforded the product (62%) which crystallised from chloroform as colourless prisms, m.p. 190°C (Found: C, 69.05; H, 6.35;N, 11.5. $C_{21}H_{23}N_3O_3$ requires C, 69.0; H, 6.35; N, 11.5%); δ8.24(dd, 1H, J7.6 and 1.4Hz, ArH), 7.57(d, 1H, J7.6Hz, ArH), 7.4(m, 2H, ArH), 6.68(m, 1H,=CH), 4.48(m, 1H,=CCHN), 3.64 and 3.47(2xm, 2x1H, CHCO), 3.32(s, 3H, NMe), 2.94(m, 3H, 3xNCH), 2.82(m, 2H, 2xNCH), 2.74(s, 3H, NMe), and 1.95(m, 4H, $2xCH_2$); m/z(%) 255(29), 254(M-N-methylmaleimide, 100), 253(17), 198(12), 184(23), 183(18) and 111(24); ν_{max}(nujol) 1680, 1620, 1580, 1450, 1180, 1090 and 750cm^{-1}.

Diels-Alder Adduct(16c). Prepared by the general procedure with a cyclisation reaction time of 3h. Preparative t.l.c. eluting with 7:3 v/v ether-methanol afforded the product (64%) which crystallised from chloroform as colourless prisms, m.p. 155°C (Found: C, 68.55; H, 7.0; N, 11.5. $C_{21}H_{25}N_3O_3$ requires C, 68.65; H, 6.85; N, 11.45%); δ8.25 and 7.6(2xd, 2x1H, ArH), 7.41(m, 2H, ArH), 6.68(m, 1H,=CH), 4.45(m, 1H,= CCHN), 3.64(m, 1H, NCH), 3.52(m, 2H, 2xCHCO), 3.31(s, 3H, NMe), 2.97(q, 4H, J7.0Hz, $\underline{CH_2}Me$), 2.74(s, 3H, NMe) and 1.13(t, 6H, J7.0Hz, $CH_2\underline{Me}$); m/z(%) 257(71), 256(M-N-methylmaleimide, 100), 241(46), 226(36), 212(43), 198(49), 197(37), 183(33) and 111(46); ν_{max} (nujol) 1690, 1630, 1590, 1470, 1170, 1075 and 740cm^{-1}.

5-Ethylidine-2-benzoxepane(19). Prepared over 16h at 80°C using catalyst A. Work up followed by preparative t.l.c. eluting with 1:9 v/v ether-petroleum ether afforded the **product** (62%) as a colourless oil (Found: C, 82.75; H, 8.05. $C_{12}H_{14}O$ requires C, 82.45; H, 8.1%); δ7.35-7.1(m, 4H, ArH), 5.76(q, 1H,=CH), 4.6(s, 2H, $ArCH_2O$), 3.95(t, 2H, J5.4Hz, CH_2O), 2.6(t, 2H, J5.4Hz, CH_2) and 1.8(d, 3H, J5.9Hz, Me); m/z(%) 174(M^+,37), 144(41), 129(100), 115(28) and 91(15).

Indoline(24) and Indole(25). Prepared at 70°C over 1h using catalyst A. Work up followed by preparative t.l.c. eluting with 3:2 v/v ether-petroleum ether afforded (24) (26%) and (25) (6%).

24. Colourless oil. HRMS: 383.1736. $C_{22}H_{25}NO_5$ requires 383.1733. δ8.36 and 8.14(2xd, 2x1H, J8.2 and 7.9Hz, ArH), 7.22 and 6.97(2xt, 2x1H, ArH), 5.79 and 5.36(2xs, 2x1H,=CH_2), 4.52(s, 2H, NCH_2), 4.21(m, 4H, 2x$\underline{CH_2}$Me), 3.09 and 2.94(2xs, 2x2H, 2xCH_2), 2.27(s, 3H, COMe) and 1.27(m, 6H, $CH_2\underline{Me}$); m/z(%) 383(M^+,100), 341(21), 309(32), 268(34), 267(74), 222(25), 195(24), 194(63) and 43(22).

25. Colourless prisms from ether-petroleum ether, m.p. 113-115°C (Found: C, 68.7; H, 6.65; N, 3.5. $C_{22}H_{25}NO_5$ requires C, 68.9; H, 6.55; N, 3.65%); δ8.45 and 7.57(2xd, 2x1H, J7.8 Hz, ArH), 7.38-7.24(m, 3H, ArH), 4.24(q, 4H, J7.1Hz, 2xOCH_2), 3.42 and 3.19(2xs, 2x2H, 2xCH_2), 2.63 and 1.79(2xs, 2x3H, $COCH_3$ and =CCH_3) and 1.28(t, 6H, J7.1Hz, 2x$CH_2\underline{Me}$); m/z(%) 383(M^+,100), 309(34), 268(29), 267(65), 194(70), 57(33) and 43(41); ν_{max} (nujol) 1720, 1700, 1250, 1220 1060 and 750cm^{-1}.

General Procedure for Triple Cyclisation of the Mannich Bases (23a-d) and (30). A mixture of Mannich base (1mmol), palladium acetate (0.1mmol), triphenylphosphine (0.2mmol), sodium formate(1.5mmol) and silver carbonate (1mmol) in dry acetonitrile (25ml) was boiled under reflux for the length of time specified in table 2. After completion of the reaction the mixture was filtered and the solvent evaporated under reduced pressure. The residue was extracted with chloroform (3x25ml), the chloroform extracts washed with water (50ml) and the combined organic extracts dried ($MgSO_4$) and concentrated. The residue was purified by flash coloumn chromatography. Yields are collected in Table 2.

Compound (25a). Purified by flash column chromatography eluting with ether. The **product** crystallised from ether-petroleum ether as colourless prisms, m.p. 78-80°C (Found: C, 70.07; H, 7.5; N, 5.7. $C_{28}H_{34}N_2O_5$ requires C, 70.25; H, 7.15; N, 5.85%); δ 7.91 - 6.92(m, 3H, ArH), 5.14(s, 2H, CH_2), 4.21(q, 4H, J7.0Hz, 2xOCH_2), 3.78(s, 2H, CH_2), 3.73(s, 2H, CH_2), 3.57(s, 2H, CH_2), 2.6-2.41(m+s, 7H, 2xCH_2 + COMe), and 1.49-1.18(m, 12H, 3xCH_2 and 2xMe); m/z(%) 478(M^+,30), 396(11), 395(38), 394(46), 393(100), 353(15), 321(35), 320(90), 278(35), 250(14), 249(14), 248(19), 206(38), 205(49), 204(47), 86(21), 84(20) and 43(37).

Compound (27b). Flash column chromatography eluting with ether followed by crystallisation from ether-petroleum ether afforded the **product** as colourless prisms, m.p. 137-139°C (Found: N, 5.65. $C_{27}H_{34}N_2O_5$ requires N, 6.0%); HRMS: 466.2460. $C_{27}H_{34}N_2O_5$ requires 466.2467. δ 7.88-6.92(m, 3H, ArH), 5.17 and 5.13(2xs, 2H, NCH_2), 4.21(q, 4H, J7.0Hz, 2xOCH_2), 3.85, 3.79 and 3.56(3xs, 3x2H, 3xCH_2), 2.51(q, 4H, J7.0Hz, 2xNCH_2), 2.54 and 2.34(2xs, 3H, COMe, amide rotational isomers), 1.26(t, 6H, J7.0Hz, 2xMe) and 1.04(t, 6H, J7.0Hz, 2xMe); m/z(%) 467(M+1,6), 396(13), 394(80), 320(100), 279(12), 74(11) and 43(36).

Compound (27c). Flash chromatography eluting with 9:1 v/v ether-methanol followed by crystallisation from ether afforded the **product** as colourless prisms, m.p. 225-227°C (Found: C, 64.7; H, 5.25; N, 7.2; S, 11.2. $C_{31}H_{31}N_3O_4S_2$ requires C, 64.9; H, 5.45; N, 7.3; S, 11.15%); δ 7.55-7.38(m, 13H, ArH), 4.98(s, 2H, CH_2), 4.78(s, 2H, CH_2), 4.53(s, 2H, CH_2), 3.60(s, 2H, CH_2), 2.30(m, 4H, 2xCH_2) and 1.43(m, 6H, 3xCH_2); m/z(%) 488(15), 432(51), 347(100), 206(80), 178(10) and 77(60).

Compound (27d). Flash column chromatography eluting with ether afforded the **product** as a colourless solid, m.p. 184-186°C (Found: C, 64.05; H, 5.3; N, 6.95. $C_{30}H_{31}N_3O_4S_2$ requires: C, 64.15; H, 5.55; N, 7.5%) δ 7.9-7.38(m, 13H, ArH), 4.99(s, 2H, CH_2), 4.79(s, 2H, CH_2), 4.53(s, 2H, CH_2), 3.72(s, 2H, CH_2), 2.42(q, 4H, J6.8Hz, 2xCH_2) and 0.98(t, 6H, J6.7Hz, 2xMe); m/z(%) 489(10), 488(23), 420(23), 347(100), 206(69) and 77(57).

Compound(30). Flash coloumn chromatography followed by crystallisation from ether-petroleum ether afforded the product as colourless prisms, m.p. 95-97°C (Found: C, 66.55; H, 6.55; N,4.85; S, 5.55. $C_{32}H_{38}N_2O_6S$ requires: C, 66.4; H, 6.6; N, 4.85; S, 5.55%); δ 8.17-7.23(m, 8H, ArH), 4.86 and 4.75(2xs, 2x2H, 2xCH_2), 4.09(q, 4H, J7.0Hz, 2xCH_2), 3.76, 3.58 and 3.37(3xs, 3x2H, 3xNCH_2), 2.45(q, 4H, J7.0Hz, 2xNCH_2), 1.10(t, 6H, J7.0Hz, 2xMe) and 1.0(t, 6H, J7.0Hz, 2xMe); m/z(%) 506(16), 505(45), 437(16), 364(100), 292(13), 281(70) and 77(14).

Diethyl 3,4-bis(methylidine)cyclopentane-1,1-dicarboxylate(32a). Piperidine (5 mol equiv) and formic acid (4mol equiv) were added to a mixture of diethyl 2-bromohept-1-en-6-yn-4,4-dicarboxylate (0.1mmol), $Pd(OAc)_2$ (0.005mmol) and triphenylphosphine(0.01mmol) in DMF (15ml). The resulting mixture was stirred and heated at 60°C for 11h. The solvent was removed under reduced pressure and the residue partitioned between ether and water. The ether layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was chromatographed on alumina eluting with 3:1 v/v petroleum ether-ether to afford the product (38%) as a colourless oil which had identical spectroscopic data to that reported previously.[22]

Diethyl 3-methylidine-4-trimethylsilylmethylidinecyclopentane-1,1-dicarboxlate(32b). Piperidine (10mol equiv) and formic acid (8mol equiv) were mixed in benzene and added to a mixture of (31b)(1mol), $Pd(OAc)_2$ (10mol%) and triphenylphosphine(20mol%) in benzene at 80°C in three portions [2xpiperidine(2.5mol equiv) and formic acid (2mol equiv) and a final portion of piperidine (5mol equiv) and formic acid (4mol equiv)] at 2h intervals. The mixture was stirred and heated for a further 9h and then worked up in the usual way. Purification by preparative t.l.c. afforded the **product** (47%) as a colourless oil (Found: C, 61.95; H, 8.4. $C_{16}H_{26}O_4Si$ requires C, 61.9; H, 8.45%); δ 6.01(t, 1H, C<u>H</u>$SiMe_3$), 5.4 and 4.94(2xt, 2x1H,=CH_2), 4.19(q, 2x2H, J7.1Hz, <u>CH_2</u>Me), 3.05 and 3.02(2xm, 2x2H, 2xCH_2) and 1.25(t, 6H, J7.1Hz, CH_2<u>Me</u>); m/z(%) 310(M^+,36), 238(38), 237(85), 236(25), 193(30), 165(27) and 164(66); ν_{max}(film) 2935, 1715, 1240, 1180 and 837cm^{-1}.

1-(4'-Methylphenylsulphonyl)-1-aza-3-methylidine bicyclo[4.3.0]nona-5-ene(35). Prepared using catalyst C in DMF at 100°C with a reaction time of 12h. Work up followed by preparative t.l.c. eluting with ether-petroleum ether afforded the **product** (50%) as a thick, pale yellow, oil. HRMS: 289.1144. $C_{16}H_{19}NO_2S$ requires 289.1136. δ 7.8 and 7.3(2xd, 2x2H, ArH), 5.8 and 5.6(2xm, 2x1H, CH=CH), 5.0 and 4.8(2xbr s, 2x1H,=CH_2), 3.9(m, 3H, NCH_2 and NCH), 2.8(m, 1H,=C-CH-C=), 2.4(s, 3H, ArMe) and 2.2-1.8(m, 4H, 2xCH_2); m/z(%) 289(M^+,66), 235(12), 155(13), 135(12), 134(100), 132(12), 118(23), 107(18), 106(6), 92(11), 91(56) and 79(23).

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