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The Synthesis of Bridged-Ring Carbo- and Hetero-cycles via Palladium Catalysed Regiospecific Cyclisation Reactions[1]

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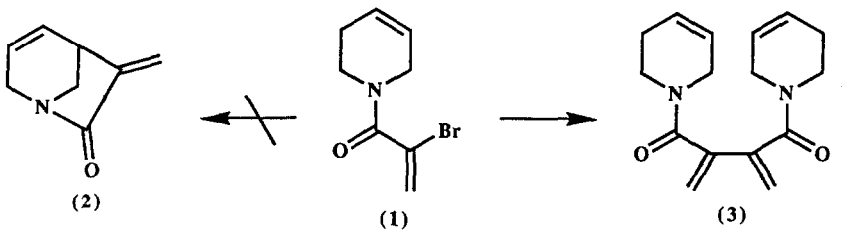
Abstract: *A catalyst system comprising 10 mol % (Pd(OAc) and 20 mol % PPh_3 effects the cyclisation of aryl halides onto proximate alkenes via 5-, 6-, and 7-exo-trig, and 7-endo-trig processes giving a variety of bridged-ring carbo- and hetero-cycles in excellent yield. Double bond isomerisation in the product is rarley encountered and may be suppressed by the addition of Tl(1) salts. One example of diastereospecific bis-cyclisation is given and the crystal structure of 1-aza-2-sulphonyl-3,4-benzobicyclo[3.2.1]nona-6-ene is reported.*

Although the Heck reaction[2] has found increasing applications in synthesis[3] and Hegedus[4] and Ban[5] illustrated the potential of the intramolecular version of the reaction for the formation of heterocycles, the reactions' potential for the construction of bridged-rings and spirocyclic systems was not appreciated until our recent studies[1,6]. Subsequently Overman[7] published similar observations and others have recently provided further examples[8] including an application to the synthesis of the 2-azabicyclo[3.3.1]nonane moiety present in strychnos alkaloids.[9]

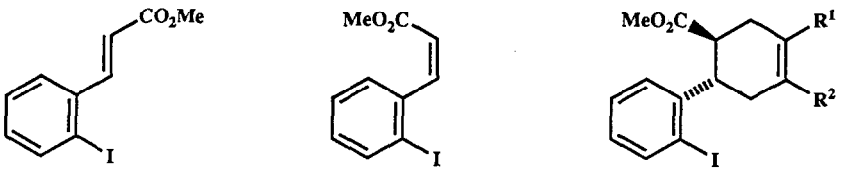
In this paper we report full details of our studies of metal catalysed 5-, 6-, and 7-exo-trig, and 7-endo-trig cyclisations producing a variety of bridged-ring products, together with an example of a bridged-ring system arising from a diastereospecific bis-cyclisation sequence. In addition the effect of Tl(1) and Ag(1) salts on certain of these processes is discussed.

5-Exo-Trig Cyclisations Our previous studies on the cyclisation selectivity (exo- versus endo-trig) of intermediate vinyl- or aryl-palladium(II) and-rhodium(II) species onto proximate alkenes established that exo-trig cyclisation is usually preferred over endo-trig cyclisation in reactions generating 5- and 6-membered rings, and that 5-membered ring formation is kinetically favoured over 6-membered ring formation, and 6- over 7-membered ring formation.[10,11] These observations all relate to fused ring formation and it was of interest to study analogous, potentially competitive, cyclisations generating bridged-rings. In all cases the catalyst system comprised 10 mol% palladium acetate and 20 mol% triphenylphosphine.

The N-acylated tetrahydropyridine(1) was prepared by the dicyclohexylcarbodiimide mediated coupling of 1,2,5,6-tetrahydropyridine and 1-bromoacrylic acid. Attempted palladium catalysed 5-exo-trig cyclisation (MeCN, 80°C, 16h) of (1) to (2) was unsuccessful. Instead the dimer (3) was obtained in 18% yield. It was felt the ring strain which would be present in (2) was probably reflected in an unfavourable cyclisation transition state and a less stained example was therefore explored.

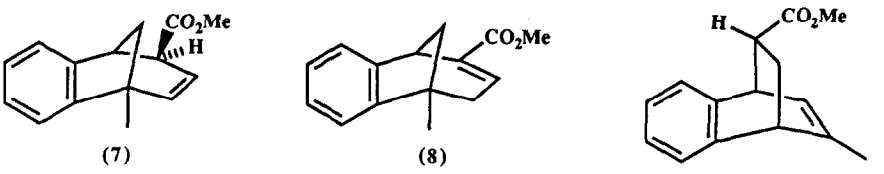


(2) (1) (3)

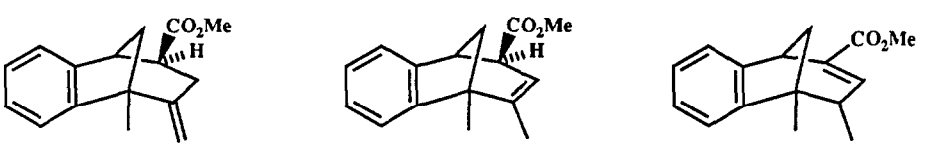


(4) (5)

(6) a. R^1= H, R^2= Me
b. R^1= R^2= Me



(7) (8) (9)



(10) (11) (12)

The Wittig reaction of 2-iodobenzaldehyde and Ph_3P-$CHCO_2Me$ afforded a 5:1 mixture of trans- and cis-isomers, (4) and (5) respectively. The Diels-Alder reactions (toluene, 125°C, sealed tube) of this mixture with isoprene and with 2,3-dimethylbutadiene afforded the Diels-Alder adducts (6a) (49%) and (6b) (70%) as single isomers with the cis-dienophile (5) being recovered from the reaction mixtures. Catalytic cyclisation of (6a) (anisole, 145°C, 22h) in the presence of potassium acetate (2 mol) required forcing conditions. The reaction was regioselective and gave a 1:8.6:1.4 mixture (66%) of (7), (8) and (9). Thus the 5-exo-trig cyclisation forming (7) and (8) predominates over the 6-exo-trig cyclisation leading to (9) and the forcing reaction conditions result in substantial double bond isomerisation with (8) being the major product. The structures of (7)-(9) are assigned on the basis of decoupling experiments. An analogous, but regiospecific, cyclisation reaction of (6b) furnished a 1:5.5:7.4 mixture of (10), (11) and (12), with the conjugated ester (12) again predominating. In both inter- and intra-molecular Heck reactions a lack of regioselectivity in the β-hydride elimination step or subsequent double bond isomerisation in the initial product sometimes severely limits the synthetic utility of the reaction. Silver(I) salts have been shown to be efficacious in controlling both these processes[12,13] and we have reported the effect of Et_4NCl, and

Ag(1) and Tl(1) salts on selectively suppressing unwanted direct capture processes[14] which sometimes compete with our newly developed palladium catalysed tandem cyclisation-anion capture processes. The success of Tl(1) salts in controlling these latter processes encouraged us to compare the effectiveness of Ag(1) and Tl(1) acetates in controlling alkene isomerisation in the cyclisation of (6b) (Table)[15].

Table. Effect of Metal Acetates on Isomer Ratios in the cyclisation of (6b)[a].

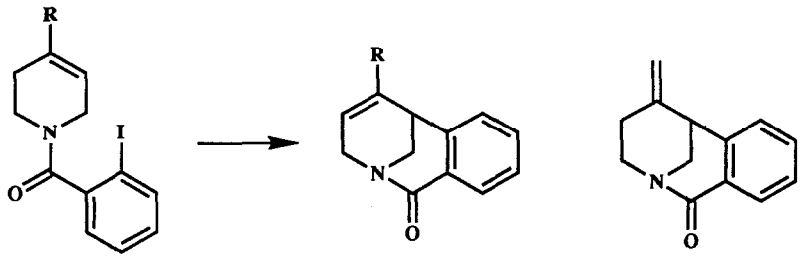
Additive(mol)	Temp(^{0}C)	Time(h)	Ratio[b]			Yield(%)
			(10)	(11)	(12)	
KOAc(2)	152	35	1	5.5	7.4	--
TlOAc(1.2)	148	12	1	1.4	c	--
TlOAc(3.8)	120	15	4.4	1	c	74
AgOAc(1.5)	135	14	1	4	0.3	--
AgOAc(4)	145	13	1	4.8	0.3	--
AgOAc(4.2)	136	12	1	4.5	0.3	79

a. All reactions carried out in anisole using 10 mol % $Pd(OAc)_2$ and 20 mol % PPh_3.
b. Isomer ratios determined by integration of the p.m.r. spectra.
c. Trace amounts of (12) present.

The reactions in which potassium acetate was replaced by TlOAc or AgOAc were noticeably faster and more selective for (10) or (11) respectively. In particular, TlOAc(3.8 mol) favours (10) over (11) by 4.4:1 whilst AgOAc(4 mol) reverses this preference and gives a 1:4.8 mixture of (10) and (11). The addition of greater than 3.8 mol of TlOAc did not result in any further improvement in the product ratio. The precise mechanism by which the Tl(1) and Ag(1) salts exercise their influence is unclear although anion exchange (RPdI + MOAc $\rightarrow$ RPdOAc + MI$\downarrow$) is clearly an important factor. It would seem reasonable that in the case of both Tl(1) and Ag(1) the initial cyclisation is followed by a β-hydride elimination favouring the conformationally unrestricted methyl group over the ring methylene group and leading to (10) as the sole or preponderant initial product. In these processes a mole of acetic acid is formed and the combination of this with Ag(1) salts (acetate and iodide) plus the high temperature could produce a Bronsted acid catalysed conversion of the exo-methylene product (10) to (11), whilst Tl(1) might moderate this effect. However, this was discounted by blank experiments in which (10) was heated at 135^{0}C in anisole in the presence of a mixture of AgOAc (3 mol), AgI(1 mol) and acetic acid (1 mol). No isomerisation was observed under these conditions or when the experiment was repeated with the

same mixture but with the addition of 10 mol % $Pd(OAc)_2$ and 20 mol % PPh_3. Cabri et al. have recently reported the beneficial effect of TlOAc in controlling the regiochemistry of coupling of aryl halides and triflates with butyl vinyl ether. Both Ag(1) and Tl(1) salts give the same regiochemistry but TlOAc is the reagent of choice.[17]

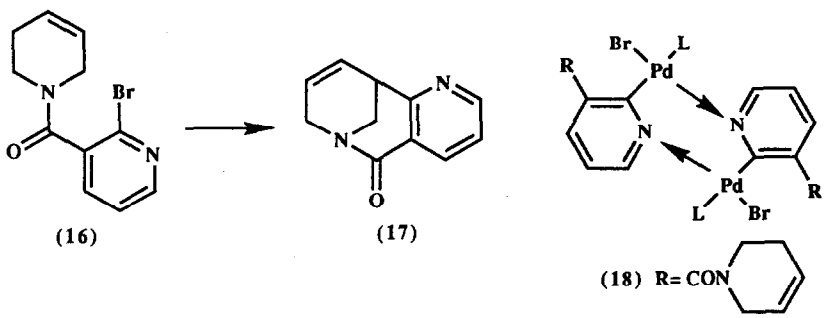
6-Exo-Trig Cyclisations. The amides (13a-c) were prepared from the corresponding 1,2,5,6-tetrahydropyridines and o-iodobenzoyl chloride and (13a,b) were cyclised to (14a,b) in boiling acetonitrile or DMF at 110-120°C in 70-90% yield, by the usual catalyst system together with potassium carbonate (2 mol) and tetraethylammonium chloride (1 mol).[18]



(13) a. R=H
b. R=Ph
c. R=Me

(14)

(15)

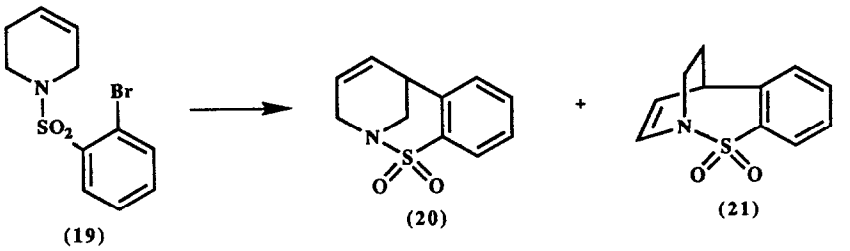


(16)

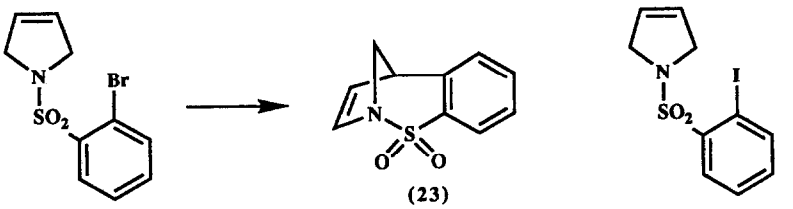
(17)

(18) R= CON

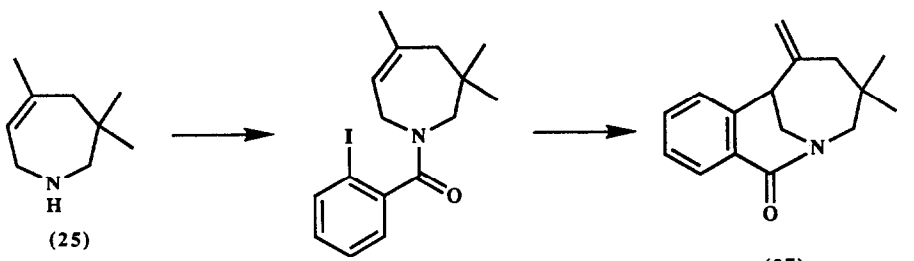
Amide (13c) cyclised (DMF, 110°C, 1.5h) to a 4:1 mixture of (14c) and (15) in 70% combined yield. No 7-endo-trig cyclisation products were detected in these cyclisation reactions. Amide (16) was prepared 1,2,5,6-tetrahydropyridine and 2-bromopyridine-3-carboxylic acid via dicyclohexylcarbodiimide mediated coupling. Compound (16) cyclised (DMF, 120°C, 3h) to (17) in moderate yield (40%) using our standard catalyst system. The need for more forcing conditions and the lower yield in this case may be due to the formation of comparatively stable dimers such as (18). Bozell has recently reported similar sluggish reactions with 2-bromopyridine.[19]



(19) (20) (21)

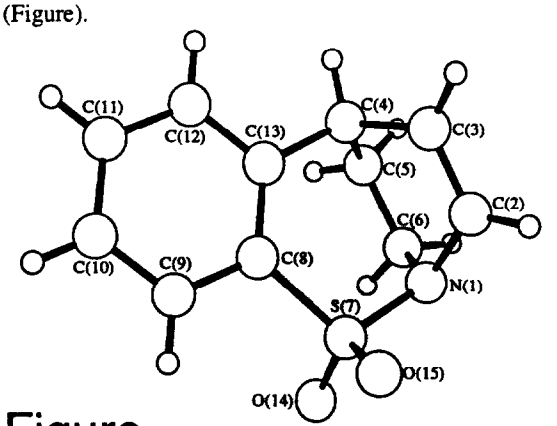


(22) (23) (24)



(25) (26) (27)

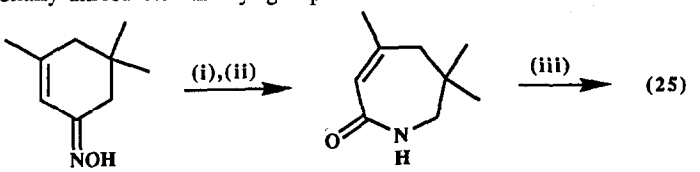
Substitution of the o-haloarylsulphonyl group for the o-haloarylacyl group produced interesting differences in reactivity and regioselectivity. Sulphonamide (19) cyclised (MeCN, 80°C, 12h) to a 1:1 mixture of (20) and (21) in 89% yield. Thus both 6-exo- and 7-endo-trig processes occur with equal facility in this case. The structure of (21) was confirmed by a single crystal X-ray structure determination (Figure).



Figure

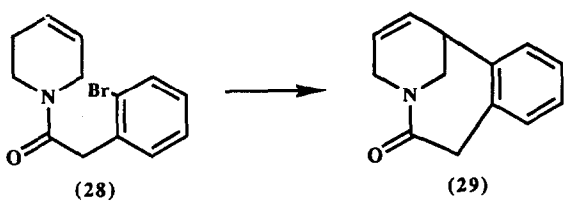
The greater steric flexibility imparted by incorporation of the SO_2 moiety was also evident in the cyclisation (MeCN, 80°C, 12h) of (22) to (23) (65%). In contrast, the N-benzoyl derivative (24) does not cyclise under these conditions.

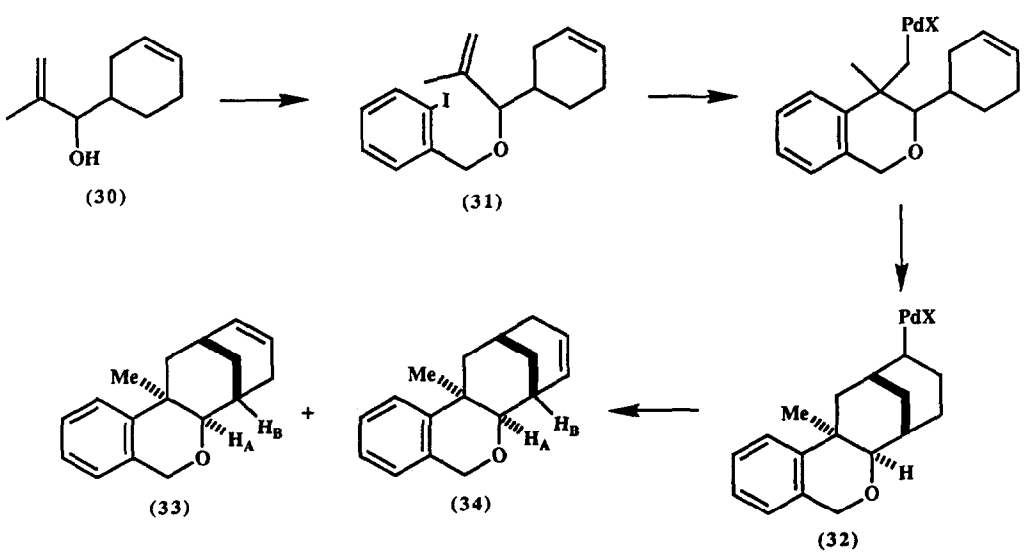
Amine (25) was prepared from isophorone oxime as outlined in Scheme 1.[20] Acylation with o-iodobenzoyl chloride afforded (26) (72%) which underwent palladium catalysed cyclisation (MeCN, 80°C, 20h) to (27) (92%). β-Hydride elimination was regiospecific and involved only the conformationally unrestricted methyl group.



Scheme 1. (i) TsOH/pyridine/16h (ii) HCl/HOAc/80°C/4.5h (iii) LiAlH4/THF/25°C/1h

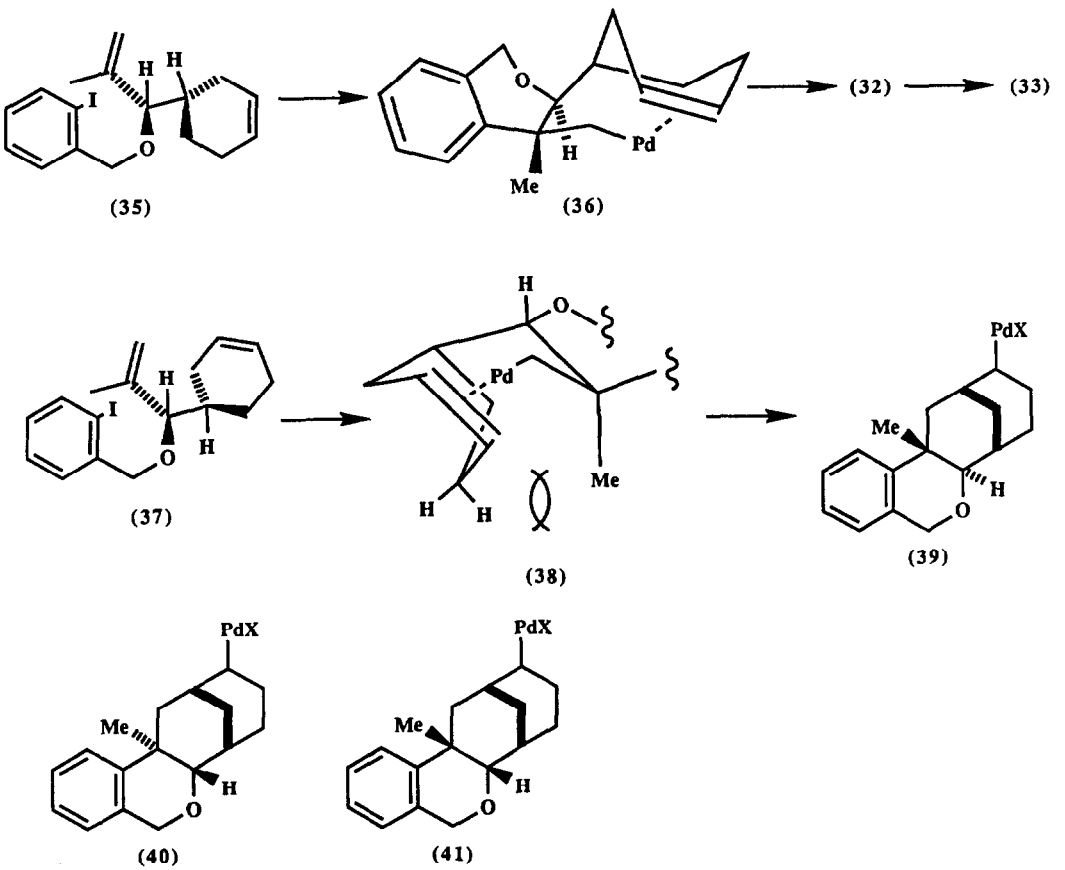
7-Exo-trig cyclisation Only one example of this process was studied. Compound (28) was prepared from 1,2,5,6-tetrahydropyridine and o-bromophenylacetylchloride in 70% yield. Cyclisation of (28) using our standard catalyst system (MeCN, 80°C, 36h) occurred by a regiospecific 7-exo-trig process giving (29) in 60% yield.





Scheme 2

Bis-cyclisation We[21] and others[22,23] have reported bis-cyclisation processes which generate both spirocyclic and fused-ring products, and Overman[22] has reported one example of a bridged-ring created in this way. We now report a further bridged-ring example. The alcohol (30)[24] reacts with o-iodobenzyl chloride to give ether (31) as a 1.2:1 mixture of diastereomers. Catalytic cyclisation (anisole, 130-140°C, 42h) of (31) afforded a 1:1.6 mixture of bridged-ring products (33) and (34) in 68% yield [based on the major diastereomer (35)]. The process proceeds via two consecutive 6-exo-trig cyclisations and involves only **one** of the diastereomeric alcohols and only **one** of two possible stereochemistries for the second cyclisation. The structures of (33) and (34) are assigned on the basis of a combination of n.O.e. and decoupling experiments.



Thus the major diastereomer (35) cyclises initially to (36, partial structure). Molecular models indicate little obvious impediment to the second cyclisation in this case. In contrast diastereomer (37) on cyclisation gives (38, partial structure) as the initial product and in this case cyclisation to either of the trans-isomers (39) or (40) is strongly impeded by a steric clash between the methyl group and one of the allylic hydrogen atoms. Similar steric interactions are apparent in the transition state leading to (41). When a 2:1 mixture of diastereomers (35) and (37) was cyclised in the presence of TlOAc (3 mol)[15] at 100°C the double bond isomerisation was partially suppressed and the product comprised a 2:1 mixture of (33) and (34).

In summary, the intramolecular Heck reaction provides efficient and rapid access to bridged ring carbo-and hetero-cyclic compounds. The cyclisation reactions are usually regiospecific but are influenced by the nature and length of the tether and the degree of substitution on the participating alkene. The bridged-ring forming bis-cyclisation process shows remarkable stereospecificity.

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.

Vinyl and Aryl Halide Precursors

1-(1'-Bromoacroyl)-1,2,5,6-tetrahydropyridine (1). A mixture of 1,2,5,6-tetrahydropyridine (1.6g, 0.02 mol), 1-bromoacrylic acid (3.1g, 0.02 mol), dicyclohexylcarbodiimide (4.12 g, 0.02 mol) and 4-dimethylaminopyridine (240 mg, 2 mmol) in methylene chloride (50 ml) was stirred at room temperature for 16h. The mixture was then filtered and the precipitated solid washed with methylene chloride. The combined filtrates were evaporated under reduced pressure and the residue purified by flash chromatography (SiO_2) eluting with 1:1 v/v ether-petroleum ether to afford the product (1.91 g, 46%) as a colourless oil (Found: C, 44.35; H, 4.75; N, 6.3. $C_8H_{16}BrNO$ requires C, 44.45; H, 4.65; N, 6.5%); δ 6.0-5.7 (M, 4H, CH=CH and C=CH_2), 4.0(br s, 2H, NCH_2CH), 3.6(m, 2H, NCH_2), and 2.2(br s , 2H, CH_2CH=); m/z(%) 215(M^+, 33), 136(100), 107(28), 82(53), 67(27) and 54(85).

Methyl *trans*-2-iodocinnamate(4) and methyl *cis*-2-iodocinnamate(5). A solution of o-iodobenzaldehyde (4.22g, 18.2 mmol) in dry methylene chloride (50 ml) was added in one portion to a stirred solution of carbomethoxymethylene triphenylphosphorane (7.11 g, 1.2 mmol) in dry methylene chloride (100 ml) at room temperature. The resulting mixture was stirred for 16h and the solvent then removed under reduced pressure, the residue triturated with petroleum ether (30 ml) and the triphenylphosphine oxide removed by filtration. Evaporation of the filtrate afforded the *product* (4.53g, 86%) as a pale yellow oil which comprised a 5:1 mixture of (4) and (5). The mixture was used for the Diels-Alder reactions (below) without further purification. A small amount of material was further purified by preparative tlc eluting with 9:1 v/v petroleum ether-methylene chloride [Found/mixed isomers): C, 41.75; H, 3.15; I, 44.05. $C_{10}H_9IO_2$ requires C, 41.7; H, 3.15: I, 44.05%]; m/z(%) (mixed isomers) 288(M^+, 6), 257(11), 162(24), 161(100), 130(26), 118(35), and 102(29).

(4) δ 7.92-6.96(m, 5H, ArH and ArCH=), 6.31(d, 1H, J 15.85Hz, C*H*CO_2Me), and 3.82(s, 3H, OMe).

(5) δ 7.92-6.96(m, 5H, ArH and ArCH=), 6.02(d, 1H, J 11.75Hz, C*H*CO_2Me) and 3.64(s, 3H, OMe).

1-Methyl-**trans**-4-methoxycarbonyl-5-(2'-iodophenyl)cyclohexene(6a). A solution of methyl 2-iodocinnamate (1.5g, 5.2 mmol) and isoprene (4.1g, 61 mmol) in dry toluene (10 ml) was placed in a sealed Carius tube and heated at 125°C for 62h. After cooling and opening the contents of the tube were evaporated under reduced pressure to afford a thick yellow oil which was purified by preparative tlc eluting with 1:3 v/v ethyl acetate-petroleum ether. The unchanges cis-iodocinnamate eluted first. The product (730 mg, 49% based on trans-iodocinnamate) was obtained as a thick colourless oil (accurate mass 356.0273, $C_{15}H_{17}IO_2$ requires 356.0275); note that the preparative t.l.c. resulted in considerable loss of product and p.m.r. indicated yields of 80-90% of (6a); δ 7.8-6.87(m, 4H, ArH), 5.47(br s, 1H, CH=), 3.6(m, 1H, ArCH), 3.47(s, 3H, OMe), 2.99(m, 1H, C*H*CO_2Me), 2.31-1.96(m, 4H, 2 x CH_2C=), and 1.72(d, 3H, J 9.63 Hz, Me); m/z(%), 356(M^+, 14), 229(100), 177(71) and 164(47).

1,2-Dimethyl-**trans**-4-methoxycarbonyl-5-(2'-iodophenyl)cyclohexene(6b). Prepared as above but using 2,3-dimethylbutadiene in place of isoprene. The product(70%) crystallised as colourless prisms, m.p. 84-86°C, from ether-petroleum ether (Found: C, 51.9; H, 5.2; I, 34.4. $C_{16}H_{19}IO_2$ requires C, 51.9; H, 5.2, I, 34.3%); δ 7.8-6.87(m, 4H, ArH), 3.47(s, 3H, OMe), 3.45(m, 1H, ArCH), 3.0(m, 1H, C*H*CO_2Me), 2.41(m, 1H, CHC=), 2.30(m, 2H, ArCHC*H*$_2$), 1.93(m, 1H, CHC=), and 1.68 and 1.64(2 x s, 2 x 3H, 2 x Me); m/z(%), 370(6), 310(11), 243(93), 217(93), 183(100), 161(51), and 153(18).

1-(2'-Iodobenzoyl)-1,2,5,6,-tetrahydropyridine (13a). A solution of 1,2,5,6-tetrahydropyridine (5g, 6.0 mmol), o-iodobenzoyl chloride (16g, 6.0 mmol) and triethylamine 6.1 mmol) in benzene (40 ml) was boiled under reflux for 1 h. The solvent was then removed under reduced pressure and the residue partitioned between methylene chloride and water. The organic layer was dried ($MgSO_4$), concentrated, and distilled to give the *product* (17g, 90.5%), b.p. 141-144°C/0.2 mm Hg as a viscous colourless oil (Found: C, 46.05; H, 3.85; N, 4.45. $C_{12}H_{12}INO$ requires C, 46.05; H, 3.85; N, 4.45%); δ 7.44(m, 4H, ArH), 5.73(m, 2H, CH=CH), 4.25 and 3.61(m, 2H, NCH_2), 3.8 and 3.29(m, 2H, NCH_2), and 2.2(m, 2H, CH_2); m/z(%), 313(M^+, 57), 231(100), 203(31), 186(48), 105(26), 77(31) and 76(47); ν_{max}(film) 3015, 2970, 2900, 2820, 1625, 1460, 1420 and 1242 cm^{-1}.

1-(2'-Iodobenzoyl)-4-phenyl-1,2,5,6-tetrahydropyridine (13b). 4-Phenyl-1,2,5,6-tetrahydropyridine hydrochloride (5.1 g, 2.6 mmol) was treated with triethylamine to liberate the free base which was dissolved in methylene chloride (100 ml), washed with water, dried ($MgSO_4$), and the solvent removed. The resulting free base was dissolved in benzene (50 ml) and o-iodobenzoyl chloride (6.7 g, 2.5 mmol) and triethylamine (5.8g, 5.7 mmol) added. The resulting solution was boiled under reflux for 1h, the solvent removed, and the residue partitioned between water and methylene chloride. The organic layer was dried ($MgSO_4$) and concentrated to give the *product* as a colourless powder (7.54g, 77%) which crystallised from ether as colourless rods (4.9g, 50%), m.p. 89.5-90.5°C. (Found: C, 55.3; H, 4.1; H, 3.6. $C_{18}H_{16}INO$ requires: C 55.55; H, 4.15; H, 3.6%); δ 7.46(m, 8H, ArH), 6.16 and 5.92(2 x brs, 2 x 1H, CH=C), 4.45(m, 1H, 1H of NCH_2C=), 3.93(m, 2H, 1H, or

$NCH_2C{=}C$ and 1H of NCH_2), 3.46(m, 1H, 1H of NCH_2), and 2.56(m, 2H, CH_2); m/z(%) 389(M^+, 98), 262(31), 231(100), 203(19), 105(57), and 77(33); ν_{max} 3025, 3010, 2940, 2910, 2810, 1618, 1570, 1438, 1232, 777 and 752 cm^{-1}.

1-(2'-Iodobenzoyl)-4-methyl-1,2,5,6-tetrahydropyridine(13c). 4-Methyl-1,2,5,6-tetrahydropyridine (960 mg, 1 mmol), and triethylamine (1.19g, 1 mmol), chloride (75 ml) were dissolved in dry methylene and cooled in an ice bath. A solution of o-iodobenzoyl chloride (2.65g, 1 mmol) in methylene chloride (10 ml) was added dropwise with stirring over 10 min. and the mixture was then allowed to warm to room temperature over 16 h. Work up in the usual way aforded the product (2.15g, 66%) as a viscous pale yellow oil, b.p. (mol still) 200°C/0.1mm Hg, which comprised a 1:1 mixture of two amide isomers. (Found: C, 48.8; H, 4.1; N, 4.1. $C_{13}H_{14}NIO$ requires C, 48.7; H, 4.3; N, 4.3%); δ (isomer A) 7.8-7.0(m, 4H, ArH), 5.45(br s, 1H, CH=), 4.32 and 4.04(2 x d, 2 x 1H, $NCH_2C{=}$), 3.28(m, 2H, NCH_2), 2.15(m, 2H, CH_2) and 1.72(s, 3H, Me); δ(isomer B) 7.8-7.0(m, 4H, ArH), 5.22(br s, 1H, CH=), 3.62 and 3.86(2 x d, 2 x 1H, $NCH_2C{=}$), 2.17(m, 2H, NCH_2), and 1.72(s, 3H, Me); m/z(%) 3.27(M^+, 72), 231(100), 200(25), 105(23), and 91(18).

1-(2'-Bromopyridyl)-1,2,5,6-tetrahydropyridine(16). A solution of 1,2,5,6-tetrahydropyridine (410 mg, 5 mmol), 2-bromonicotinic acid (1.01g, 5 mmol), dicyclohexylcarbodiimide (1.03g, 5 mmol), and 4-dimethylaminopyridine (60 mg, 0.5 mmol) in methylene chloride (10 ml) was stirred at room temperature for 3 h. The precipitated urea was filtered off and the filtrate evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2) eluting with 1:1 v/v ether-petroleum ether to afford the product (780 mg, 59%) which crystallised from ether-petroleum ether as colourless needles, m.p. 219-221°C(d) (Found: C, 49.35; H, 4.15; N, 10.5. $C_{11}H_{11}BrN_2O$ requires C, 49.45; H, 4.15; N, 10.5%); δ 8.4-7.3(m, 3H, ArH), 6.0-5.5(m, 2H, CH=CH), 4.4-3.3(m, 4H, 2 x NCH_2) and 2.2(m, 2H, CH_2); m/z(%) 268/266(M^+, 38), 186/184(61), 158/156(31), 99(48) and 56(100).

1-(2'-Brombenzenesulphonyl)-1,2,5,6-tetrahydropyridine(19). Prepared by the same procedure as that used for (13c) but using 2-bromobenzenesulphonyl chloride as the sulphonylating agent. The *product* (73%) crystallised from ether-petroleum ether as pale yellow prisms, m.p. 58-60°C (Found: C, 44.0; H, 4.2; N, 4.6. $C_{11}H_{12}BrNO_2S$ requires C, 43.7; H, 4.0; N, 4.65%), δ 8.13-7.36(m, 4H, ArH), 5.8 and 5.6(2 x m, 2 x m, 2 x 1H, CH=CH), 3.8(br t, 2H, $NCH_2C{=}$), 3.4(t, 2H, NCH_2) and 2.2(br t, 2H, CH_2); m/z(%) 303/301(29), 221/219(16), 155/157(16) and 82(100).

1-(2'-Bromobenzenesulphonyl)-3-pyrroline(22). Prepared in analogous manner to that described above from 3-pyrroline and 2-bromobenzenesulphonyl chloride. The product (66%) crystallised as colourless prisms from ether-petroleum ether, m.p. 67-69°C. (Found: C, 41.4; H, 3.5; N, 5.05. $C_{10}H_{10}BrNO_2S$ requires C, 41.65; H, 3.45; N, 4.85%); δ 8.0-7.4(m, 4H, ArH), 5.8(s, 2H, CH=CH), and 4.3(s, 4H, 2 x NCh_2); m/z(%), 289/287(30), 156/154(35), 132(11) and 68(100).

2,5,6,7-Tetrahydro-4,6,6-trimethylazepine(25). 2-Oxo-4,6,6-trimethyl-1,4,5,6-tetrahydroazepine (20 g, 0.13 mol) was added to a stirred suspension of lithium aluminium hydride (2.5g, 0.66 mol) in dry THF(50 ml) under an atmosphere of nitrogen. The mixture was stirred at room temperature for

1h, cooled to 0°C and then treated, by dropwise addition, with water (2.5 ml), 15% sodium hydroxide solution (2.5 ml) and water (7.5 ml). The inorganic salts were removed by filtration and washed with ether (3 x 20 ml). The combined organic layers were further diluted with ether (75 ml), dried ($MgSO_4$) and concentrated to afford the product (15 g, 83%), as a mobile brown oil, b.p. 32-35°/0.5 mm Hg, which was converted to the hydrobromide salt, m.p. 149-151°C. (Found (hydrobromide salt): C, 49.35; H, 8.3; N, 6.4. $C_9H_{18}BrN$ requires C, 49.1; H, 8.2; N, 6.35%); δ(free base), 5.61(t, 1H, CH=), 2.75(s, 2H, NCH_2CMe_2), 2.09(s, 2H, CH_2C=), 1.71(s, 3H, MeC=), 1.54(br s, 1H, NH), and 0.89(s, 6H, 2 x Me); m/z(%)(free base) 139(M^+, 52), 124(100), 95(70), 84(22), 82(51), 68(25) and 67(29).

1-(2'-Iodobenzoyl)-2,5,6,7-tetrahydro-4,6,6-trimethylazepine(26). Prepared from (25) using the same procedure as that used for (13c) above. The product (72%) was obtained as a thick pale yellow oil by preparative tlc eluting with 3:7 v/v petroleum ether-ether and comprised a 1:1 mixture of amide isomers. Accurate mass 369.05911, $C_{16}H_{20}NOI$ requires 369.05913. δ(isomer A) 7.8-7.0(m, 4H, ArH), 5.83(t, 1H, CH=), 4.58 and 4.06(dd and d, 2 x 1H, NCH_2C=), 3.2(dd, 2H, NCH_2), 1.74(s, 2H, CH_2C=), and 1.09 and 0.78(2 x s, 2 x 3H, 2 x Me); δ(isomer B) 7.8-7.0(m, 4H, ArH), 5.3(t, 1H, CH=), 3.57(dd, 2H, NCH_2C=), 2.34(m, 2H, NCH_2), 1.74(s, 2H, CH_2C=), and 1.08 and 0.77(2 x s, 2 x 3H, 2 x Me); m/z(%), 369(M^+, 51), 242(18), 231(100), 123(25) and 91(46); ν_{max}(film) 1650(br), 1580, 1420 and 1300 cm^{-1}.

1-(2'-Bromophenylacetyl)-1,2,5,6-tetrahydropyridine(28). Prepared from 1,2,5,6-tetrahydropyridine and 2-bromophenylacetyl chloride using the same procedure as for (13c) above. The product (70%) crystallised as colourless prisms from ether-petroleum ether, m.p. 57-59°C(Found: C, 55.35; H, 4.9; N, 4.85. $C_{13}H_{14}BrNO$ requires C, 55.7; H, 5.0; N, 5.0%); the product consisted of a 1:1 mixture of amide isomers in $CDCl_3$, δ(isomer A) 7.8-7.2(m, 4H, ArH), 6.2-5.7(m, 2H, CH=CH), 4.3(t, 2H, NCH_2C=), 4.0(s, 2H, NCH_2CO), 3.6(t, 2H, NCH_2) and 2.2(br m, 2H, CH_2C=); δ(isomer B), 7.8-7.2(m, 4H, ArH), 6.2-5.7(m, 2H, CH=CH), 4.1(t, 2H, NCH_2C=), 3.95(s, 2H, $ArCH_2$), 3.9(t, 2H, NCH_2), and 2.3(br m, 2H, CH_2C=), m/z(%) 303/301(M^+, 31), 221/219(6), 157/155(16), 55(80) and 54(61).

Allylic ether (31). 4-(1'-Hydroxy-2'-methylprop-2-enyl)cyclohexene (2.5 g, 10 mmol) was dissolved in dry DMF(75 ml) and sodium hydride (0.5 g, 50% in mineral oil) added portionwise with stirring. The mixture was stirred for a further 1 h and then a solution of o-iodobenzyl chloride (2.52g, 10 mmol) in dry DMF (10 ml) was added dropwise over 15 min. The resulting mixture was stirred overnight at room temperature. The solvent was then removed under reduced pressure and the residue partitioned between ether (75 ml) and water (60 ml). The water layer was extracted with ether (75 ml) and the combined ether extracts dried (Na_2SO_4) and evaporated. The residual oil was distilled to afford the product (2.6 g, 54%) as a colourless oil, b.p. 140-144°C/0.2 mmHg, which comprised a ca. 1.2:1 mixture of diastereomers (35) and (37). (Found: C, 55.9; H, 6.0. $C_{17}H_{22}IO$ requires C, 55.45; H, 5.7%); δ(**35**) 7.8-7.0(m, 4H, ArH), 5.7(m, 2H, CH=CH), 5.10 and 4.93(2 x br s, 2H, $C=CH_2$), 4.46 and 4.24(2 x d, 2 x 1H, J 11.5 Hz, $ArCH_2$), 3.55(d, 1H, CHO), 2.7-1.0[m, 6H, $(CH_2)_3$], and 1.7(s, 3H, Me); δ(**37**) 7.8-7.0(m, 4H, ArH), 5.7(m, 2H, CH=CH), 5.07 and 4.95(2 x br s, 2H, $C=CH_2$), 4.47 and 4.26(2 x d, 2 x 1H, J 11.5Hz, $ArCH_2$), 3.5(d, 1H, CHO), 2.4-1.0[m,

6H, $(CH_2)_3$] and 1.5(s, 3H, Me); m/z(%)(mixed isomers) 368(M^+, 1), 287(11), 217(100) and 134(65).

Palladium Catalysed Cyclisations

General Procedure for Amide Cyclisations. A mixture of the bromo- or iodo-amide (2 mmol), palladium acetate (0.2 mmol), triphenylphosphine (0.4 mmol), tetraethylammonium chloride (2 mmol) and anhydrous potassium carbonate (4 mmol) in dry acetonitrile (80 ml) was boiled under reflux under an atmosphere of dry nitrogen until tlc monitoring showed that all the starting material had been consumed. The mixture was then filtered to remove inorganic salts 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.

5-Exo-Trig Cyclisations

Buta-1,3-diene-2,3-bis(1′,2′,5′,6′-tetrahydropyridylcarboxamide)(3). Work up after 16 h followed by crystallisation from ether-petroleum ether afforded the product (18%) as colourless needles, m.p. 150-151°C(Found: C, 71.0; H, 7.9; N, 10.25. $C_{16}H_{20}N_2O_2$ requires C, 70.55; H, 7.4; H, 10.3%); δ(ca. 5:3 mixture of amide isomers) 5.7(m, 4H, 2 x CH=CH), 5.35(m, 4H, 2 x $C=CH_2$), 4.2-3.5(4 x s, 8H, 4 x NCH_2), and 2.2(d, 4H, 2 x $CH_2C=$); m/z(%), 272(M^+, 1), 190(28), 163(26), 136(44), and 82(100).

Cyclisation of Diels-Alder Adducts (6a,b)

General Procedure A solution of the Diels-Alder adduct (1 mmol), palladium acetate (0.1 mmol), triphenylphosphine (0.2 mmol), and potassium acetate (2 mmol) in anisole (60 ml) was heated with stirring at 140°C for 26-30h. The reaction mixture was then filtered and the filtrate evaporated under reduced pressure. The residual oil was dissolved in methylene chloride (30 ml), washed with water (2 x 50 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was then purified by preparative tlc.

In reactions summarised in the Table in the text potassium acetate was replaced by AgOAc or TlOAc as appropriate.

Cyclisation of 1-methyl-**trans**-4-methoxycarbonyl-5-(2′-iodophenyl)cyclohexane(6a). The reaction was worked up after 26 h and the 8.6:4:1 mixture of isomeric products (7)-(9) was separated by preparative tlc eluting with 7:3 v/v ether-petroleum ether (Found (mixed isomers): C, 78.8; H, 7.2. $C_{15}H_{16}O$ requires C, 78.9; H, 7.1%); m/z(%)(mixed isomers) 228(M^+, 87), 196(40), 169(52), 168(100), 153(36) and 128(22).

(7) Colourless oil. δ 7.3-7.0(m, 4H, ArH), 6.0(dd, 1H, C<u>H</u>=CH, J 1.93 and 11.43 Hz), 5.33(m, 1H, CH=C<u>H</u>), 3.76(s, 3H, OMe), 3.64(br s, 1H, ArCH), 3.10(br s, 1H, CHC=), 2.11(m, 2H, CH_2), and 1.45(s, 3H, Me).

(**8**) Colourless oil. δ 7.27-7.06(m, 4H, ArH), 6.56(m, 1H, CH=), 3.96(d, 1H, J 4.4 Hz, ArCH), 3.74(s, 3H, OMe), 2.45 and 2.12(2 x dd, 2 x 1H, J 4.4 and 19.7 Hz, CH_2C=), and 2.12 and 1.84(2 x m, 2 x 1H, CH_2).

(**9**) Colourless oil. δ 7.3-7.0(m, 4H, ArH), 6.38(d, 1H, CH=), 3.75(m, 1H, ArCH), 3.75(s, 3H, OMe), 3.64(br s, 1H, ArCH), 3.01(br s, 1H, C<u>H</u>CO_2Me), 2.33 and 1.24(2 x m, 2 x 1H, CH_2) and 1.46(s, 3H, Me).

<u>Cyclisation of 1,2-dimethyl-**trans**-4-methoxycarbonyl-5-(2'-iodophenyl)cyclohexene(6b)</u>. The reaction was carried out by the general procedure and worked up after 30 h. to afford a 1:5.5:7.9 mixture (80%) of (10)-(12) which was separated by preparative tlc eluting with 1:9 v/v ether-petroleum ether (Found (mixed isomers): C, 79.3; H, 7.5. $C_{16}H_{18}O_2$ requires C, 79.3; H, 7.5%); m/z(%) (mixed isomers) 242(M^+, 98), 227(30), 210(88), 195(77), 183(100), 182(95), 167(94), and 129(84).

(**10**) Pale yellow oil. δ 7.32-7.0(m, 4H, ArH), 4.83 and 4.70(2 x s, 2 x 1H, C=CH_2), 3.73(s, 3H, OMe), 3.63(m, 1H, ArCH), 2.72(m, 1H, C<u>H</u>CO_2Me), 2.56(d, 1H, CHC=, J 15.3 Hz), 2.04(dd, 1H, bridge H, J 4.95 and 11.0 Hz), 1.79(d, 1H, bridge H, J 11.1 Hz), 1.75(m, 1H, CHC=), and 1.49(s, 3H, Me).

(**11**) Pale yellow oil. δ(m, 4H, ArH), 4.959m, 1H, CH=), 3.74(s, 3H, OMe), 3.57(m, 1H, ArCH), 2.97(m, 1H, C<u>H</u>CO_2Me), 2.17 and 2.03(d and m, 2 x 1H, bridge CH_2), and 1.71 and 1.42(2 x s, 2 x 3H, 2 x Me).

(**12**) Pale yellow oil. δ 7.39-7.0(m, 4H, ArH), 6.41(d, 1H, CH=), 3.96(m, 1H, ArH), 3.73(s, 3H, OMe), 2.14(m, 1H, C<u>H</u>Me), 1.93 and 1.92(2 x s, 2 x 1H, bridge CH_2), 1.39(s, 3H, Me), and 1.16(d, 3H, Me).

<u>1-Aza-2-oxo-3,4-benzobicyclo[3.3.1]nona-6-ene(14a)</u>. Prepared by the amide cyclisation procedure detailed above and with a reaction time of 1 h. The <u>product</u> (80%) was obtained as a colourless oil, b.p. (mole still) 100°C/0.2 mmHg(Found: C, 77.95; H, 5.9; N, 7.55. $C_{12}H_{11}NO$ requires C, 77.8; H, 6.0; N, 7.5%); δ 7.49(m, 4H, ArH), 5.88 and 5.59(2 x m, 2 x 1H, CH=CH), 4.25 and 3.75(dd, 2 x 1H, J 18.0 Hz, NCH_2), 3.68 and 3.44(2 x dd, 2 x 1H, J 13.0 Hz, NCH_2), and 3.03(br s, 1H, ArCH); m/z(%) 185(M^+, 75), 184(28), 156(19), 129(12), 128(19), and 42(100); ν_{max}(film) 3040, 2930, 1660, 1590, and 1370 cm^{-1}.

<u>1-Aza-2-oxo-3,4-benzo-6-phenylbicyclo[3.3.1]nona-6-ene(14b)</u>. Prepared by the amide cyclisation procedure with a reaction time 24 h. The <u>product</u> (54.5%) crystallised from ether as colourless rods, m.p. 154-156°C (Found: C, 82.75; H, 5.85; N, 5.5. $C_{18}H_{15}NO$ requires C, 82.75; H, 5.8; N, 5.35%); δ 7.47(m, 9H, ArH), 5.86(m, 1H, CH=C), 4.48(dd, 1H, NCH), 4.39(m, 2H, one H of NCH_2C= and one H of $NC\underline{H}_2CH$); m/z(%) 261(M^+, 75), 220(24), 184(8), 105(16), 102(6), 101(11), and 42(100); ν_{max} 3038, 3002, 2920, 2880, 1648, 1610, 1590, 1448, 1350 and 1242 cm^{-1}.

1-Aza-2-oxo-3,4-benzo-6-methylbicyclo[3.3.1]nona-6-ene(14c) and 1-aza-2-oxo-3,4-benzo-6-methylene bicyclo[3.3.1]nona-6-ene(15). Prepared by the standard amide procedure but with DMF as solvent and a temperature of 120°C for 1.5h. The product (74%) was a thick yellow oil which comprised 1:4 mixture of (14c) and (15). The mixture was separated by preparative tlc eluting with 7:3 v/v ether-petroleum ether. Accurate mass (mixed isomers) 199.0998 $C_{13}H_{13}NO_3$ requires 199.0997; m/z(%)(mixed isomers) 199(M^+, 55), 170(29), 157(25), 128(12) and 42(100); ν_{max}(film) (mixed isomers) 1670, 1600, 1370 and 1250 cm^{-1}.

(**14c**) Colourless oil. δ 7.9-7.2(m, 4H, ArH), 5.02(s, 1H, CH=C), 4.26(d, 1H, NCHC=), 3.76(d, 2H, NCH_2), 2.86(s, 1H, ArCH), and 1.7(s, 3H, Me).

(**15**) Colourless oil. δ 7.9-7.2(m, 4H, ArH), 5.05 and 4.76(2 x s, 2 x 1H, $C=CH_2$), 4.09(dd, 1H, $NCHCH_2$, J 6.3 and 12.9 Hz), 3.76(d, 1H, NCHCH, J 12.6Hz), 3.48(s, 1H, ArCH), 3.3(dd, 1H, NCHCH, J 12.3 and 1.8 Hz), 3.12 and 2.07(m and dd, 2 x 1H, $CH_2C=$) and 2.5(m, 1H, $NCHCH_2$).

1-Aza-2-oxo-[3,4-b]pyridylbicyclo[3.3.1]nona-6-ene(17). Prepared by the standard amide cyclisation procedure but in DMF at 120°C for 4h. The product (40%) was obtained as colourless needles from ether-petroleum ether, m.p. 70°C (Found: C, 71.05; H, 5.6; N, 14.85. $C_{11}H_{10}N_2O$ requires C, 70.95; H, 5.4; N, 15.05%); δ 8.5-7.3(m, 3H, ArH), 6.1 and 5.7(2 x m, 2 x 1H, CH=CH), 4.4(m, 1H, ArCH), 3.9(m, 2H, NCH_2) and 3.6 and 3.4(m and d, 2 x 1H, NCH_2); m/z(%) 186(M^+, 100), 157(40), 130(25) and 42(40).

1-Aza-2-thia-3,4-benzobicyclo[3.3.1]nona-6-ene 2,2-dioxide(20) and 1-aza-2-thia-3,4-benzobicyclo[3.2.2]nona-6-ene 2,2-dioxide(21). Prepared by the standard amide cyclisation procedure with a reaction time of 12 h. Purification by preparative tlc afforded the product (89%) as a colourless solid, m.p. 104-107°, which comprised a 1:1 mixture of (20) and (21) [Found(mixed isomers): C, 58.95; H, 4.85; N, 6.15. $C_{11}H_{11}NO_2S$ requires C, 59.4; H, 4.95; N, 6.35%); m/z(%) (mixed isomers) 339(M^+, 100), 221(57), 130(20), 129(54), 128(67), and 42(27). Careful crystallisation of the mixture from methylene chloride-petroleum ether afforded a small amount of pure (21). The p.m.r. data for (20) is derived from the spectrum of a mixture.

(**20**) δ 7.8-7.18(m, 4H, ArH), 6.2 and 5.6(br t and br d, 2 x 1H, CH=CH), 4.4(t, 2H, NCHH and NCHC=), 4.0(dd, 1H, NCHC=, J 9.7 and 1.7 Hz), 3.6(dd, 1H, NCHH, J 14.1 and 2.0 Hz), and 3.2(d, 1H, ArCH).

(**21**) Colourless prisms, m.p. 153-155°C. δ 7.8-7.18(m, 4H, ArH), 6.8 and 6.5(t, and d, 2 x 1H, CH=CH), 4.2 and 3.6(m, and t, 2 x 1H, NCH_2), 3.4(m, 1H, CH), and 2.3(m, 2H, CH_2).

1-Aza-2-thia-3,4-benzobicyclo[3.2.1]octa-6-ene 2,2-dioxide(23). Prepared by the general amide procedure with a reaction time of 16h. Preparative tlc eluting with 2:3 v/v ether-petroleum ether afforded the product (65%) which crystallised from ether-petroleum ether as colourless prisms, m.p. 147-148°C (Found: C, 58.05; H, 4.3; N, 6.95. $C_{10}H_9NO_2S$ requires C, 57.95; H, 4.35; N, 6.75%); δ 7.7-7.1(m, 4H, ArH), 6.6 and 6.4(t and d, 2 x 1H, CH=CH), 4.49(d, 1H, NCHH, J 11.87 Hz),

4.05(dd, 1H, NCHH, J 3.96 and 11.87 Hz), and 3.31(t, 1H, CHC=); m/z(%). 207(M^+, 5), 115(100), 89(13) and 63(12).

1-Aza-2-oxa-3,4-benzo-6-methylene-8,8-dimethylbicyclo[4.3.1]decane(27). Prepared by the general amide cyclisation procedure with a 12 h reaction time. After purification by preparative tlc, eluting with ether-petroleum ether, the product (91%) was obtained as a viscous pale yellow oil (Found: C, 79.5; H, 8.0; N, 5.85. $C_{16}H_{19}NO$ requires C, 79.65; H, 7.95; N, 5.8%); δ 8-7.3(m, 4H, ArH), 5.01 and 4.84(2 x s, 2 x 1H, $C=CH_2$), 4.36 and 3.7(2 x d, 2 x 1H, $NCHHCMe_2$ and NCHHCH), 3.55(d, 1H, $NCHHCMe_2$, J 13.6Hz), and 1.03 and 0.85(2 x s, 2 x 3H, CMe_2); m/z(%) 241(M^+, 100), 199(15), 198(21) and 91(7); ν_{max}(film) 2930, 1660(br), 1600 and 1410 cm^{-1}.

1-Aza-2-oxa-4,5-benzobicyclo[4.3.1]deca-7-ene(29). Prepared by the general amide cyclisation procedure with a 36 h reaction time. Preparative tlc, eluting with 2:3 ether-petroleum ether, followed by crystallisation from ether-petroleum ether afforded the product (60%) as colourless plates, m.p. 117-119°C(Found: C, 78.5; H, 6.6; N, 7.0. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.55; N, 7.05%); δ 7.3-7.0(m, 4H, ArH), 5.8 and 5.6(m, dd, 2 x 1H, CH=CH), 4.6(br d, 1H, ArCH), 4.4(2 x d, 2H, NCH_2), 3.6-3.2(m, 4H, NCH_2 and $COCH_2$); m/z(%), 199(M^+, 100), 170(30), 128(40) and 42(20).

Bis-cyclisation of Allylic Ether (31)

a. Cyclisation of a 1.2:1 mixture of diastereomers (35) and (37) was carried out by the general procedure used for the Diels-Alder cycloadducts (anisole, 140°C, 42h). Work up followed by preparative tlc eluting with 1:18 ether-petroleum ether afforded the product (68%) [based on (35)] as a thick pale yellow oil which comprised a 1:1.6 mixture of double bond isomers (33) and (34). (Found (mixed isomers): C, 84.8; H, 8.5. $C_{17}H_{20}O$ requires C, 85.0; H, 8.35%); m/z(%) (mixed isomers) 240(M^+, 98), 147(82), 146(59), 145(43), 131(68) and 129(33). The endo-orientation of the ring junction Me and H_A protons is assigned on the basis of a positive Me/H_A n.O.e. of 3-4% in both isomers and a near zero H_A/H_B coupling constant in both isomers.

(**33**) δ 7.3-6.9(m, 4H, ArH), 6.0 and 5.7(2 x m, 2 x 1H, CH=CH), 4.77(s, 2H, CH_2O), 3.52(s, 1H, H_A), 2.6(br s, 1H, H_B) and 2.48-1.2(m, 7H, 3 x CH_2 and CH).

(**34**) δ 7.3-6.9(m, 4H, ArH), 6.0 and 5.8(m and dt, 2 x 1H, CH=CH), 4.76(s, 2H, CH_2O), 3.5(s, 1H, H_A), 2.5(br s, 1H, H_B), and 2.48-1.2(m, 7H, 3 x CH_2 and CH).

b. Cyclisation of a 2:1 mixture of diastereomers (35) and (37) in anisole (100°C, 24h), using the general procedure but with thallium acetate (3 mmol) replacing potassium acetate, afforded the *product* (67.5%) [based on (35)] as a 2:1 mixture of (33) and (34).

Single crystal X-ray diffraction analysis of **21** - All crystallographic measurements were carried out at 200 K on a Stoe STAD14 diffractometer using graphite monochromated Molybdenum K_α X-radiation (λ=71.069 pm). Data were collected in the range of $4.0^0 < 2\theta < 50.0^0$ over 22.6 hours

using θ-0 scans with no significan variation in the intensities of three standard reflections. Lorentz and polarisation corrections were applied to the data-set together with a semi-empirical absorption correction using azimuthal psi-scans. The structure was solved by direct methods using SHELXS[25] and was refined by full-matrix least-squares using SHELX76.[26] All non-hydrogen atoms were refined with anisotropic thermal parameters. The phenyl group was treated as a rigid body with idealised hexagonal symmetry (C-C = 139.5 pm). All hydrogen atoms were included in calculated positions (C-H = 96 pm) and were refined with an overall isotropic thermal parameter. The weighting scheme $w=[\sigma^2(F_o)^2 + 0.0004(F_o)^2]^{-1}$ was used. *Crystal data* - $C_{11}H_{11}NO_2S$, M = 221.28, orthorhombic, space group $P2_12_12_1$, a=903.8(1), b=948.8(1), c=1229.4(2) pm, U=1.0542(2) nm^3, Z = 4, D_x=1.39 Mg m^{-3}, μ=2.72 cm^{-1}, $F(000)$=464. *Data collection* - Scan speeds 1.5 - 8.0° min^{-1}, ω scan widths 1.4° + α-doublet splitting, $4.0<2\theta<50.0^0$, 1112 Data collected, 1003 with $I>1.0\sigma(I)$ considered observed. *Structure refinement* - Number of parameters = 125, R=0.0414, R_w=0.0540.

Table A Selected bond lengths (pm) angles (°) for 21 with e.s.d.'s in parantheses.

C(2)-N(1)	144.7(6)	C(6)-N(1)	150.4(9)
S(7)-N(1)	163.3(5)	C(3)-C(2)	134.7(8)
C(4)-C(3)	150.4(10)	C(5)-C(4)	152.7(9)
C(13)-C(4)	153.4(7)	C(6)-C(5)	144.9(8)
C(8)-S(7)	175.5(4)	O(14)-S(7)	141.9(4)
O(15)-S(7)	142.6(4)		
C(6)-N(1)-C(2)	111.9(5)	S(7)-N(1)-C(2)	112.8(4)
S(7)-N(1)-C(6)	115.6(4)	H(2)-C(2)-N(1)	121.7(3)
C(3)-C(2)-N(1)	116.7(5)	C(3)-C(2)-H(2)	121.7(4)
H(3)-C(3)-C(2)	121.5(4)	C(4)-C(3)-C(2)	116.9(5)
C(4)-C(3)-H(3)	121.5(3)	H(4)-C(4)-C(3)	108.7(3)
C(5)-C(4)-C(3)	108.6(5)	C(5)-C(4)-H(4)	109.8(3)
C(13)-C(4)-C(3)	112.6(5)	C(13)-C(4)-H(4)	105.5(3)
C(13)-C(4)-C(5)	111.6(5)	H(5a)-C(5)-C(4)	108.2(4)
H(5b)-C(5)-C(4)	108.2(4)	H(5b)-C(5)-H(5a)	109.5*
C(6)-C(5)-C(4)	114.5(5)	C(6)-C(5)-H(5a)	108.2(4)
C(6)-C(5)-H(5b)	108.2(4)	C(5)-C(6)-N(1)	113.3(5)
H(6a)-C(6)-N(1)	108.5(4)	H(6a)-C(6)-C(5)	108.5(4)
H(6b)-C(6)-N(1)	108.5(4)	H(6b)-C(6)-C(5)	108.5(4)
H(6b)-C(6)-H(6a)	109.5*	C(8)-S(7)-N(1)	107.7(2)
O(14)-S(7)-N(1)	107.7(3)	O(14)-S(7)-C(8)	107.7(2)
O(15)-S(7)-N(1)	107.2(3)	O(15)-S(7)-C(8)	108.1(3)
O(15)-S(7)-O(14)	118.0(3)	C(9)-C(8)-S(7)	115.2(2)
C(13)-C(8)-S(7)	124.8(2)	C(8)-C(13)-C(4)	123.4(3)
C(12)-C(13)-C(4)	116.6(3)		

* idealised angles

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