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THE SYNTHESIS OF SPIROCYCLIC COMPOUNDS BY REGIOSPECIFIC PALLADIUM CATALYSED CYCLISATION REACTIONS[1]

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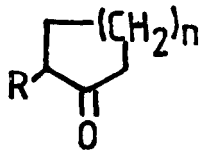
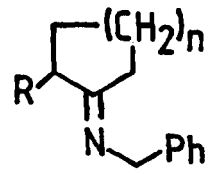
Abstract. Enamides derived from o-iodobenzoic acid and Z-3-bromoacrylic acid undergo regiospecific palladium catalysed exo-trig cyclisation onto a proximate alkene to give spirocyclic products in good to excellent yield. Double bond isomerisation in the product is not usually observed and is retarded by the addition of tetraethylammonium chloride which also allows the reaction to be carried out under milder conditions.

We have been studying the cyclisation selectivity (exo- versus endo-:rig) of intermediate vinyl-palladium(11) and - rhodium(111) species onto)roximate double bonds.[2-4] Exo-trig cyclisation is usually preferred over :ndo-trig cyclisation in the absence of severe steric effects, and five-iembered ring formation is kinetically favoured over six-membered ring :ormation. Thus in most cases the cyclisation can be achieved regio-;pecifically. When the initial vinyl-palladium species is formed by)xidative addition of a vinyl- or aryl-halide or - triflate these cyclisation)rocesses are examples of the intramolecular Heck reaction[5]. The intra-nolecular Heck reaction[6] has been extensively studied for the synthesis of ieterocycles, notably by Hegedus[7] and Ban[8]. However only simple ring forming processes had been studied prior to our work and the reaction's)otential for the construction of bridged-rings, tetrasubstituted carbon :entres or spirocyclic systems had not been appreciated. We now describe our studies of the latter process in detail.[1]

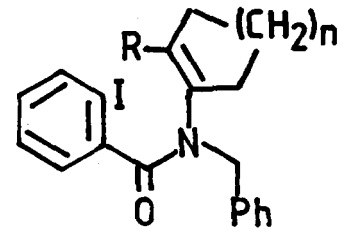
Initially we studied the palladium catalysed cyclisation of a series of enamides of 2-iodobenzoic acid. These were prepared from the corresponding ketones (1) via the imines (2) which on treatment with o-iodobenzoyl



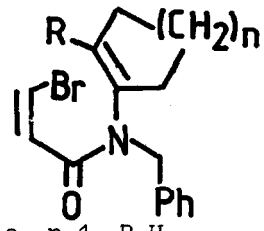
(1) n = 1-4
R=H or CO_2Et



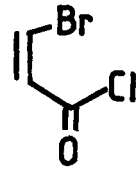
(2) n=1-4
R=H or CO_2Et



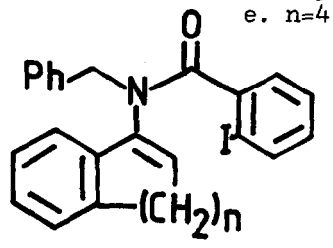
(3) a. n=1, R=H
b. n=1, R=CO_2Et
c. n=2, R=H
d. n=3, R=H
e. n=4, R=H



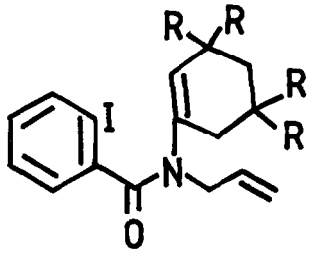
(4) a. n=1, R=H
b. n=1, R=CO_2Et
c. n=2, R=H
d. n=2, R=CO_2Et
e. n=3, R=H



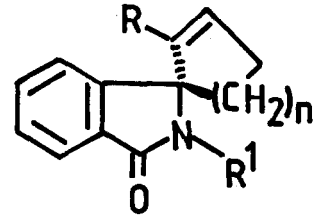
(5)



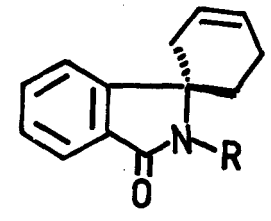
(6) a. n=1
b. n=2
c. n=3



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



(8) a. n=1,R=H, R^1=CH_2Ph
b. n=1,R=CO_2Et,R =CH_2Ph
c. n=2,R=H, R^1=CH_2Ph
d. n=3,R=H, R^1=CH_2Ph
e. n=4,R=H, R^1=CH_2Ph
f. n=2,R=H, R^1= $CH_2CH=CH_2$



(9) a. R=CH_2Ph
b. R= $CH_2CH=CH_2$

chloride in benzene at 80°C in the presence of triethylamine afforded the enamides (3a-e). An analogous series of enamides (4a-e) was prepared by acylating the imines (2) with (5). Both series of enamides are sensitive to moisture and were often used directly for the cyclisation studies without further purification. Two other series of enamides, (6a-c) and (7a,b), were prepared in an analogous manner.

The enamides (3a-e) undergo smooth regiospecific 5-exo-trig cyclisation on heating at 45-80°C in acetonitrile containing anhydrous potassium carbonate as base, tetraethylammonium chloride (1mol), and 10 mol % palladium acetate and 20 mol. % triphenylphosphine as catalyst. The spirocyclic products (8a-e) are obtained in good yield, usually as single isomers (Table) In the case of (3c) cyclisation at 80°C in the absence of tetraethylammonium chloride resulted in a 1.3:1 mixture (60%) of (8c) and (9a). In the presence of tetraethylammonium chloride (3c) cyclised slowly at 45°C to give a 3.8:1 mixture (76%) of (8c) and (9a). The use of a tetra-alkylammonium chloride to facilitate palladium catalysed vinylation of organic halides was introduced to Jeffrey[9]. Halberg[10] and later Overman[11] have employed silver salts to promote Heck reactions and reduce double bond isomerisation. The enamide (3e), in addition to (8e), also gave a small amount (ca. 5%) of an isomeric spirocyclic product.

The cyclisation of enamides (4a-e), which were all carried out in the presence of tetraethylammonium chloride (1mol)(Table), also proceed regiospecifically via a 5-exo-trig process. The spirocyclic products (10a-e) are obtained in moderate to good yield and in these cases no products arising from double bond isomerisation were detected.

The enamides (6a-c) cyclised more slowly than (4a-e) but gave the corresponding spirocyclic products in good yield (Table). Enamide (6a) gave (11) in excellent yield whilst (6b) gives a 4.25:1 mixture of (13a) and (12a) in the presence of tetraethylammonium chloride. Enamide (6c) underwent cyclisation in excellent yield but this was accompanied by extensive double bond isomerisation even in the presence of tetraethylammonium chloride (Table). The product consisted of a 1:1.95:4.86 mixture of (12b), (14) and (13b).

In the preceding examples the cyclisation could proceed by a 5-exo- or 6-endo-trig process. In all cases they proceed via the 5-exo-trig mode and no products arising from 6-endo-trig cyclisations were detected. Cyclisation of the enamides (7a) and (7b) offers the possibility of competition between 5-exo-, 6-endo-, 6-exo-, and 7-endo-trig cyclisation modes. In (7b) the 5-exo-trig mode, if it occurs, cannot lead to product due to the absence of a β-hydride elimination pathway for the intermediate alkylpalladium species. Such species can however be intercepted by hydride ion sources, organotin

compounds etc.[4] In the presence of tetraethylammonium chloride and the palladium acetate-triphenylphosphine catalyst system (7a) cyclises mainly by the 5-exo-trig route to give a 9:1 mixture of (8f, 9b), and (15a). The latter arises via a 6-exo-trig cyclisation process. The ratio of (8f) to (9b) was 1:1. As expected, (7b) cyclises solely via the 6-exo-trig process.

Table. Cyclisation of enamides (3a-e), (4a-e), (6a-c) and (7a,b) to spirocyclic products[a]

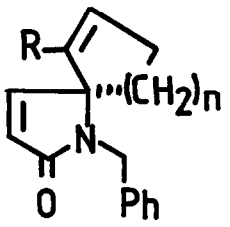
Enamide	Temp. (°C)	Time (h)	Product	Yield (%)
3a	80	2.5	8a	60[b]
3b	80	2.0	8b	70
3c	45	72	8c,9a	67[c]
3d	45-50	48	8d	71
3e	45-50	48	8e	75
4a	80	1.5	10a	50
4b	80	2.0	10b	80
4c	80	3.0	10c	55
4d	80	3.0	10d	37
4e	80	6.0	10e	75
6a	80	12.0	11	87
6b	80	10.0	12a,13a	62[d]
6c	80	24.0	12b,13b,14	94[e]
7a	80	9.0	8f,9b,15a	52[f]
7b	80	36.0	15b	50

a. All reactions carried out in acetonitrile containing anhydrous potassium carbonate (2mol) and tetraethylammonium chloride (1mol) with 10mol% palladium acetate and 20mol% triphenylphosphine as catalyst.
b. No Et_4NCl (1mol) added.
c. Product consists of a 3.8:1 mixture of (8c) and (9a).
d. Product consists of a 4.25:1 mixture of (13a) and (12a).
e. Product consists of a 1:1.95:4.86 mixture of (12b), (14) and (13b).
f. Product consists of 4.5:4.5:1 mixture of (8f), (9b) and (15a).

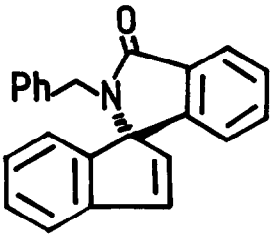
Cyclisation is slow (3 days) at 50°C and results in a 1:1.75 mixture (50%) of (15b) and (16). When the reaction is carried out at 80°C (15b) is the sole product (Table).

This new cyclisation complements the work of Ninomiya and co-workers who photocyclised N-benzoyl enamines of cyclohexanones via a 6-endo process[12]. Overman and co-workers subsequently developed the intramolecular

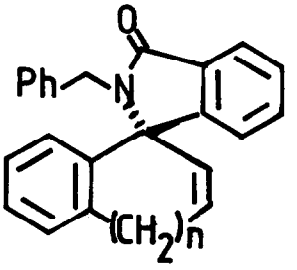
Heck reaction as one of several possible approaches to the spiro-oxindole alkaloid gelsamine and have demonstrated the spirocyclisation process, albeit in poor yield, for a 7-exo-trig example.[11] Analogous radical cyclisations giving spiro-oxindoles have also been reported[13] but in these cases small amounts of 6-endo-trig cyclisation products are formed.



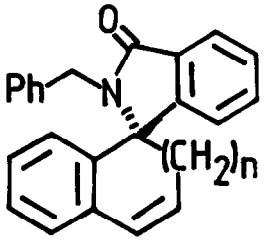
(10) a. n=1, R=H
b. n=1, R=CO_2Et
c. n=2, R=H
d. n=2, R=CO_2Et
e. n=3, R=H



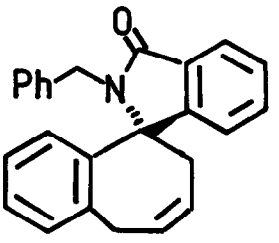
(11)



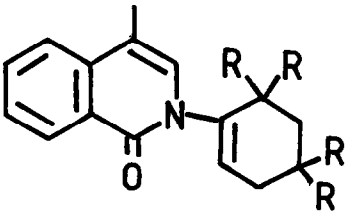
(12) a. n=1
b. n=2



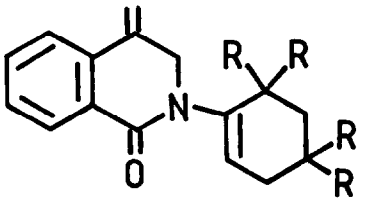
(13) a. n=1
b. n=2



(14)



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



(16)

Experimental General experimental details were as previously noted.[2] Petroleum ether refers to the fraction with b.p. 40-60°C. Infrared spectra were determined for thin films unless otherwise stated. Imines were prepared by literature methods[14,15] except as noted below.

Imines

General Procedure. A solution of the cyclic ketone (0.1 mol) and benzylamine (0.1 mol) in benzene (200ml) was boiled under reflux for 3-12h with water

removal by a Dean-Stark trap. After completion of the reaction the yellow solution was concentrated under reduced pressure and the residual oil distilled under vaccuo to afford the pure imine.

N-Cyclooctylidene benzylamine. Obtained (70%) as a pale yellow oil, b.p. 110-114°C/0.05 mmHg (Found: C, 83.85; H, 9.80; N, 6.75. $C_{15}H_{21}N$ requires C, 83.65; H, 9.85; N, 6.50%); δ 7.1 (s, 5H, ArH), 4.4 (s,2H,NCH_2) and 2.6-1.5 (m, 14H, 7 x CH_2); m/z(%) 215 (M^+,19), 187(10), 105(8) and 91(100).

N-3,3,5,5-Tetramethylcyclohexylidene allylamine. Obtained (60%) as a colourless oil, b,p. 40°C/0.1mmHg (Found: N, 7.05. $C_{13}H_{23}N$ requires N, 7.25%); δ 5.8 (m,1H,C<u>H</u>=CH_2), 5.0 (m,2H,CH=C<u>H</u>$_2$), 4.0 (d,2H,NCH_2), 2.2 (s,4H,2xCH_2), 1.6 (s,2H,CH_2) and 1.2 (s,12H,4xMe); m/z(%) 193 (M^+,10), 178(56) and 84(100).

Benzylamine imine of 1-benzosuberone. Prepared according to the general method but with the addition of dibutyltin dichloride (5 mol %) as a catalyst The product (55%) distilled as a pale yellow thick oil, b.p. 142-148°C/ 0.2mmHg, whose p.m.r. spectrum (below) showed it to comprise a 2:1 mixture of stereoisomers. (Found: C, 86.70; H, 7.55; N, 5.35. $C_{18}H_{19}N$ requires C, 86.70; H, 7.70; N, 5.60%); δ 7.5-7.0 (m,9H,ArH), 4.7 and 4.47 (2xs, 2H, NCH_2 of E- and Z-isomers), 2.7 (m,4H, 2xCH_2) and 1.75 (m,4H,2xCH_2); m/z(%) 249 (M^+,62), 248(41), 206(26), 160(47), 131(30), 104(22) and 91(100).

Enamides

(a) General Procedure for o-Iodobenzoylenamides. A mixture of the imine (1mmol), o-iodobenzoyl chloride (1mmol) and triethylamine (1mmol) in dry benzene (80ml) was boiled under reflux for 1-2h. The reaction mixture was then cooled, diluted with benzene (50ml), washed with brine (50ml), and then water (50ml). The benzene solution was dried (Na_2SO_4) and concentrated to afford the crude enamide which was used directly for the cyclisation reaction. In some cases where water sensitivity was a particular problem the water and brine washes were omitted and the benzene solution was filtered to remove triethylammonium chloride. The filtrate was then concentrated under reduced pressure and the residue used directly for the cyclisation step

(b) General Procedure for Z-3-Bromoacryloyl Enamides. A solution of Z-3-bromoacryloyl chloride (1mmol) in dry benzene (20ml) was added dropwise with stirring to a solution of the imine (1mmol) and triethylamine (1mmol) in dry benzene (50ml) over ca. 15 min. at room temperature. The resulting mixture was stirred overnight and then filtered. The filtrate was diluted with benzene (50ml) and washed with water, dried, and evaporated under reduced pressure to afford the crude enamide which was used directly for the cyclisation step without further purification.

I-Benzyl-N-(cyclopent-1-enyl)-2-iodobenzamide (3a). The product (72%) was a thick yellow oil which decomposed on attempted distillation. δ 7.7-6.7 m,9H,ArH), 5.66 (t,1H, =CH), 4.82 (br s, 2H, NCH_2) and 2.0-0.8 m,6H,3xCH_2); m/z(%) 403(M^+,2), 248(50), 231(76) and 91(100).

I-Benzyl-N-(2-carboethoxycyclopent-1-enyl)-2-iodobenzamide (3b). Obtained 80%) as a thick yellow oil which decomposed on attempted distillation. δ 8.0-7.4 (m,9H,ArH), 5.0 (br s, 2H,NCH_2), 4.4 (q,2H,$\underline{CH_2}$Me), 2.4-1.0 m,6H,3xCH_2) and 1.4 (t,3H,$CH_2\underline{Me}$); m/z(%) 479 (M^+,1), 348(20), 231(90) and 91(100).

I-Benzyl-N-(cyclohex-1-enyl)-2-iodobenzamide (3c). Obtained (62%) as colourless prisms from ether-petroleum ether, m.p. 62°C (Found: C, 57.60; H, 4.65 N, 3.15. $C_{20}H_{20}INO$ requires C, 57.55; H, 4.85; N, 3.35%); δ 7.73-6.8 m, 9H, ArH), 5.44 (m,1H,=CH), 4.76 (br s, 2H, NCH_2) and 2.14-1.0 m,6H,3xCH_2); m/z(%) 417 (M^+,21), 303(10), 290(24), 231(95) and 91(100).

N-Benzyl-N-(cyclohept-1-enyl)-2-iodobenzamide (3d) The product (80%) was a thick yellow oil which decomposed on attempted distillation. A small sample was further purified by preparative t.l.c. (SiO_2) eluting with 1:1 v/v ether-petroleum ether to afford a colourless oil (Found: C, 58.50; H, 5.25; N, 3.45. $C_{21}H_{22}INO$ requires C, 58.40; H, 5.10; N, 3.25%); δ 7.66-6.82 m,9H,ArH), 5.58 (t,1H, =CH), 4.71 (br s,2H,NCH_2) and 2.0-1.0 (m, 10H, 5 x CH_2); m/z(%) 431 (M^+,24), 340(13), 276(14), 231(53), 200(19) and 91(100).

N-Benzyl-N-(cyclooct-1-enyl)-2-iodobenzamide (3e). Obtained (71%) as a thick yellow oil which decomposed on attempted distillation. δ 7.8-7.0 (m,9H,ArH), 5.6 (t,,1H, =CH), 4.8 (br s, 2H,NCH_2) and 2.2-1.0 (m,12H,6xCH_2); m/z(%) 445 (M^+,8), 318(40), 231(9) and 91(100).

N-Benzyl-N-(cyclopent-1-enyl)-Z-3-bromoacrylamide (4a). Obtained (60%) as colourless plates from ether-hexane, m.p. 58-60°C (Found: C, 58.60; H, 5.30; N, 4.95. $C_{15}H_{16}BrNO$ requires C, 58.85; H, 5.25; N, 4.55%); δ 7.19-7.21 (m,5H,ArH), 6.77 and 6.56 (2xd, 2x1H, J 8Hz, BrCH=CHCO), 5.35 (m,1H, =CH), 4.57 (s,2H, NCH_2), 2.23 (m,4H, 2x =CCH_2) and 1.80 (m,2H,CH_2); m/z(%) 307, 305 (M^+,1), 226(25), 198(6) and 91(100); ν_{max}(KBr) 3065, 3030, 2851, 1641, 1399, 1239 and 1180.

N-Benzyl-N-(2-carboethoxycyclopent-1-enyl)-Z-3-bromoacrylamide (4b). Obtained (66%) as a thick yellow oil. Accurate mass: 377.0627. $C_{18}H_{20}BrNO_3$ requires 377.0627. δ 7.2-7.0 (m,5H,ArH), 6.55 and 6.01 (2xd, 2x1H, J 9.6Hz, BrCH=CHCO), 5.06 and 4.50 (2xd, 2x1H, J 15.7Hz, NCH_2), 3.92 (q,2H,$\underline{CH_2}$Me), 2.5-1.6 (m,6H,3xCH_2) and 1.08 (t,3H,$CH_2\underline{Me}$); m/z(%) 379,377 (M^+,3), 333(23), 297(15), 270(16), 224(35) and 91(100); ν_{max}(CCl_4) 3065, 3032, 2981, 2938, 1727, 1674, 1638, 1611 and 1388 cm^{-1}.

N-Benzyl-N-(cyclohex-1-enyl)-Z-3-bromoacrylamide (4c). Obtained (70%) as a thick yellow oil. Accurate mass: 319.0571. $C_{16}H_{18}BrNO$ requires 319.0572.

δ 7.2-7.4 (m,5H,ArH), 6.79 and 6.58 (2xd, 2x1H, J 8Hz, BrCH=CHCO), 5.41 (m,1H, =CH), 4.66 (s,2H,NCH_2), 2.30 (t,1H, J 6.6Hz) and 2.0-1.4 (m,7H); m/z(%) 321, 319 (M^+,0.5), 240(39) and 91(100); $\nu_{max.}$ 3069, 2935, 1637 and 1494 cm^{-1}.

N-Benzyl-N-(2-carboethoxycyclohex-1-enyl)-Z-3-bromoacrylamide (4d). Obtained (47%) as a thick yellow oil. Accurate mass: 392.0710. $C_{19}H_{22}BrNO_3$ requires 392.0783. δ 7.16-7.23 (m,5H,ArH), 6.71 and 6.55 (2xd, 2x1H, J 8Hz, BrCH=CHCO), 4.93 and 4.24 (2xd, 2x1H, J 14.5Hz, NCH_2), 3.91 (q,2H,CH_2Me), 2.25 and 1.87 (2xm, 2x2H, $=CCH_2$), 1.46 (m,4H,2xCH_2) and 1.10 (t, 3H, CH_2Me); m/z(%) 393,391 (M^+,0.5), 220(18), 318(18), 312(20) and 91(100); $\nu_{max.}$(CCl_4) 2940, 2863, 1710, 1658, 1447, 1389, 1281 and 1245 cm^{-1}.

N-Benzyl-N-(cyclohept-1-enyl)-Z-3-bromoacrylamide (4e). Obtained (47%) as a thick yellow oil. Accurate mass: 333.0727. $C_{17}H_{20}BrNO$ requires 333.0729. δ 7.24-7.12 (m,5H,ArH), 6.76 and 6.50 (2xd, 2x1H, J 8Hz, BrCH=CHCO), 5.44 (t,1H,=CH), 4.59 (s,2H,NCH_2) and 2.11-1.32 (m, 10H, 5 x CH_2); m/z(%) 335,333 (M^+,0.5), 254(40) and 91(100); $\nu_{max.}$ 3031, 2925,1643 and 1397 cm^{-1}.

N-Benzyl-N-(inden-1-yl)-2-iodobenzamide (6a). The product (70%) was a thick yellow oil which decomposed on attempted distillation. δ 7.68-6.8 (m,13H,ArH), 6.08 (s,1H,=CH), 5.09 (br s, 2H,NCH_2) and 3.0 (s,2H,=CHCH_2); m/z(%) 451 (M^+,3), 360(13), 325(25), 324(91) and 91(100).

N-Benzyl-N-(1,2-dihydronaphth-4-yl)-2-iodobenzamide (6b). The product (68%) crystallised from ether-petroleum ether as colourless needles, m.p. 115-116°C (Found: C, 62.00; H, 4.25; N, 2.95. $C_{24}H_{20}INO$ requires C, 61.95; H, 4.30; N, 3.00%); δ 7.8-6.9 (m,13H,ArH), 6.2 (s,1H, =CH), 4.9 (s,2H,NCH_2) and 2.8-2.0 (M,4H,2xCH_2); m/z(%) 465 (M^+,27), 337(15), 231(63), 117(50) and 91(100).

N-Benzyl-N-(benzocyclohept-1-enyl)-2-iodobenzamide (6c). A solution of o-iodobenzoyl chloride (2.66g, 1mmol) in dry benzene (15ml) was added dropwise to a stirred and ice cooled solution of benzosuberone benzylamine imine (2.49g, 1mmol) and triethylamine (1.01g, 1mmol) in dry benzene (30ml). The resulting mixture was stirred at room temperature for 16h, filtered to remove triethylammonium chloride and then worked up as for the general procedure. The crude product was purified by flash chromatography (SiO_2) eluting with 3:7 v/v ether-petroleum ether. The enamide (6c) (3.65g, 76%) was obtained as a colourless amorphous solid, m.p. 30-32°C, from ether-petroleum ether (Found: C, 62.35; H, 4.60; N, 2.95. $C_{25}H_{22}INO$ requires C, 62.65; H, 4.60; N, 2.90%); δ 7.72-6.84 (m,13H,ArH), 5.97 (t,1H,=CH), 5.20 (s,2H,NCH_2), 1.85 (m,4H,2xCH_2) and 1.57 (m,2H,CH_2); m/z(%) 479 (M^+,22), 388(51), 231(100), 248(75), 203(33), 159(29), 131(56) and 91(86); $\nu_{max.}$(KBr) 3040, 3020, 2930, 2855, 1645 and 1390 cm^{-1}.

N-Allyl-N-(cyclohex-1-enyl)-2-iodobenzamide (7a). The product (50%) was obtained as a pale yellow oil by molecular distillation, b.p. 180°C/0.1mmHg (Found: C, 51.90; H, 4.90; N, 3.65. $C_{16}H_{18}INO$ requires C, 52.30; H, 4.90; N, 3.80%); the p.m.r. specrum showed the presence of isomers arising from the amide bond. δ (major) isomer 7.79-6.90 (m,4H,ArH), 5.99 (m,1H,CH=CH_2), 5.70 (t,1H, ring =CH), 5.30 (m,2H,CH=CH_2) 4.2 (d, 2H, NCH_2) and 1.9-1.0 (m,8H,4xCH_2); δ (minor isomer) 7.96-6.90 (m,4H,ArH), 5.99 (m,1H,CH=CH_2), 5.73 (t,1H, ring =CH), 5.25 (m,2H,CH=CH_2) 3.78 (d,2H,NCH_2) and 2.19-1.0 (m,8H,4xCH_2); m/z(%) 367 (M^+,8), 231(100) 212(25), 203(21) and 105(8).

N-Allyl-N-(3,3,5,5-tetramethylcyclohex-1-enyl)-2-iodobenzamide (7b). The product (72%) crystallised from ether-petroleum ether as colourless prisms, m.p. 60-62°C (Found: C, 57.00; H, 6.25; N, 3.60. $C_{20}H_{26}INO$ requires C, 56.75; H, 6.20; N, 3.30%); δ 7.9-6.9 (m,4H,ArH), 5.94 (m,1H, CH=CH_2), 5.48 (s,1H, ring =CH), 5.23 (m,2H,CH=CH_2), 4.2 (br s, 2H,NCH_2), 1.75 (s,2H, =CHCH_2), 1.05 (s,2H,CH_2) and 0.78 (2xs, 2x6H, 4xMe); m/z(%) 423 (M^+,11), 408(57), 231(100) and 41(28).

Spirocyclic Compounds

General Procedure for Cyclisation Reactions. A mixture of the enamide (0.5mmol), palladium acetate (0.05mmol), triphenylphosphine (0.1mmol), anhydrous potassium carbonate (1mmol) and tetraethylammonium chloride (0.5mmol) in dry acetonitrile (80ml) was heated at the temperature, and for the length of time, shown in the Table. After completion of the reaction the mixture was filtered to remove inorganic salts and filtrate evaporated under reduced pressure. The residue was dissolved in ether and filtered through a short column of silica eluting with ether. Removal of the ether afforded the crude product which was purified by crystallisation or preparative t.l.c. as appropriate. Yields are given in the table.

Spirocycle (8a). Obtained as colourless prisms from ether-petroleum ether, m.p. 75-78°C (Found: C, 82.70, H, 6.25; N, 5.05. $C_{19}H_{17}NO$ requires C, 82.90; H, 6.20; N, 5.10%); δ 7.89-7.19 (m,9H,ArH), 6.18 and 5.25 (2 x m, 2x1H, CH=CH), 4.80 and 4.40 (2xd, 2x1H, J 15.6Hz, NCH_2) and 2.58 and 2.10 (2xm, 2x2H, 2xCH_2); m/z(%) 275 (M^+,100), 246(22), 184(25), 170(54), 142(14) and 91(46); $\nu_{max.}$ (KBr) 1675, 1470 and 1400 cm^{-1}.

Spirocycle (8b). Obtained as colourless plates from methylene chloride-petroleum ether, m.p. 98-100°C. Accurate mass: 347.1516. $C_{22}H_{21}NO_3$ requires 347.1521. δ 7.9-7.21 (m,10H,ArH and =CH), 4.77 and 4.44 (2xd, 2x1H, J 15.5Hz, NCH_2), 3.70 (m,2H,CH_2Me), 2.65 and 2.36 (2xm, 2x2H, 2xCH_2) and 0.82 (t,3H, CH_2Me); m/z(%) 347 (M^+,100), 293(14), 242(91), 185(55) and 169(58); $\nu_{max.}$ (KBr) 1720, 1680, 1470 and 1390 cm^{-1}.

Spirocycles (8c) and (9a). The mixed isomers crystallised from ether-petroleum ether as colourless prisms, m.p. 121-123°C. [Found (mixed isomers): C, 82.80; H, 6.60; N, 5.1. $C_{20}H_{19}NO$ requires C, 83.00; H, 6.60; N, 4.85%]; m/z(%)(mixed isomers) 289 (M^+,100), 246(30), 235(28), 234(13), 198(28) and 91(73).

8c δ 7.9-7.19 (m,9H,ArH), 6.13 (m,1H, =C<u>H</u>CH$_2$), 5.13 (d,1H, J 10Hz, CC<u>H</u>=CHCH$_2$), 4.91 and 4.45 (2xd, 2x1H, J 15.8Hz, NCH$_2$) and 2.55-1.63 (m,6H,3xCH$_2$).

9a δ 7.9-7.19 (m,9H,ArH), 5.87 and 5.80 (2xm, 2x1H, CH=CH), 4.88 and 4.67 (2xd, 2x1H, J 15.8Hz, NCH$_2$) and 2.55-1.63 (m,6H,3xCH$_2$).

Spirocycle (8d). Obtained as colourless needles from ether-petroleum ether, m.p. 123-124°C (Found: C, 83.15; H, 7.15; N, 4.45. $C_{21}H_{21}NO$ requires C, 83.15; H, 7.00; N, 4.60%); δ 7.97-7.20 (m,9H,ArH), 5.95 (m,1H, =C<u>H</u>CH$_2$), 5.05 (d,1H, J 12Hz, CC<u>H</u>=CHCH$_2$), 4.95 and 4.50 (2xd, 2x1H, J 15.7Hz, NCH$_2$) and 2.37-1.4 (m,8H,4xCH$_2$); $\nu_{max.}$ (KBr) 1690, 1500, 1400 and 1360 cm^{-1}.

Spirocycle (8e). Obtained as colourless prisms from ether-petroleum ether, m.p. 90-92°C. Accurate mass: 317.1779. $C_{22}H_{23}NO$ requires 317.1786.

7.95-7.18 (m,9H,ArH), 5.95 and 5.57 (2xm, 2x1H, CH=CH), 4.90 and 4.78 (2xd, 2x1H, J 16.1Hz, NCH$_2$) and 2.28-1.66 (m,10H,5xCH$_2$); m/z(%) 317 (M^+,3), 235(4), 226(3) and 91(15).

Spirocycle (10a). Obtained as colourless prisms from ether-petroleum ether, m.p. 58-60°C (Found: C, 79.80; H, 6.70; N, 6.25. $C_{15}H_{15}NO$ requires C, 79.95; H, 6.70; N, 6.20%); δ 7.28-7.22 (m,5H,ArH), 6.89 and 6.15 (2 x d, 2x1H, J 5.8Hz, CH=CHCO); 6.07 and 5.14 (2xm, 2x1H, CH=CH), 4.67 and 4.24 (2xd, 2x1H, J 15.6Hz, NCH$_2$), 2.42 (m,2H,CH$_2$) and 1.99 and 1.76 (2 x m, 2x1H, CH$_2$); m/z(%) 225 (M^+,62), 134(15), 120(76) and 91(100).

Spirocycle (10b). Obtained as a pale yellow oil by preparative t.l.c. (Found: N, 4.75. $C_{18}H_{19}NO_3$ requires N, 4.70%); accurate mass: 297.1363. $C_{18}H_{19}NO_3$ requires 297.1364. δ 7.25 (m,5H,ArH), 6.64 and 6.10 (2 x d, 2x1H, CH=CHCO), 5.19 (t,1H,=CH), 4.96 and 4.85 (2xd, 2x1H, J 15.3Hz, NCH$_2$), 4.01 (q,2H,<u>CH$_2$Me</u>), 2.58-1.89 (m,4H,2xCH$_2$) and 1.11 (t,3H,CH$_2$<u>Me</u>); m/z(%) 297 (M^+,27), 225(10), 224(53) and 91(100); $\nu_{max.}$ (CCl_4) 3031, 2980, 2935, 1729, 1670, 1608 and 1229 cm^{-1}.

Spirocycle (10c). Obtained as colourless plates from ether-petroleum ether, m.p. 62-64°C (Found: N, 5.65. $C_{16}H_{17}NO$ requires N, 5.85%); accurate mass: 239.1309. $C_{16}H_{17}NO$ requires 239.1310; δ 7.27 (m,5H,ArH), 7.05 and 6.15 (2xd, 2x1H, J 6Hz, CH=CHCO), 6.0 and 5.0 (2xm, 2x1H, CH=CH), 4.8 and 4.25 (2xd, 2x1H, J 15.8Hz, NCH$_2$) and 2.2-1.5 (m,6H,3xCH$_2$); m/z(%) 239 (M^+,100), 134(89), 106(14), 92(12) and 91(91); $\nu_{max.}$ 3020, 2920, 1680, 1640(sh), 1390 and 815 cm^{-1}.

Spirocycle (10d). Obtained as colourless prisms from ether-petroleum ether,

.p. 86-88°C (Found: C, 73.90; H, 6.85; N, 4.75. $C_{19}H_{21}NO_3$ requires , 73.30; H, 6.80; N, 4.50%); δ 7.27 (m,5H,ArH), 6.45 and 6.05 (2 x d, 2 x 1H, H=CHCO), 5.26 (t,1H,=CH), 5.43 and 4.40 (2xd, 2x1H, J 15.9Hz, NCH_2), 4.12 q,2H,$\underline{CH_2}Me$), 2.41-1.66 (m,6H,3xCH_2) and 1.22 (t,3H,$CH_2\underline{Me}$); m/z(%) 311 M^+,25), 239(11), 238(54), 220(37), 148(22) and 91(100).

pirocycle (10e). Obtained as a thick pale yellow oil by preparative t.l.c. Found: C, 80.80; H, 7.30; N, 5.80. $C_{17}H_{19}NO$ requires C, 80.55; H, 7.55; , 5.55%); δ 7.18 (m,5H,ArH), 7.05 and 6.08 (2xd, 2x1H, J 5.9Hz, CH=CHCO), .84 and 4.91 (2xm, 2x1H, CH=CH), 4.74 and 4.23 (2xd, 2x1H, J 15.6Hz, NCH_2) 2.22-1.26 (m,8H,4xCH_2); m/z(%) 253 (M^+,81), 162(18), 148(29) & 91(100).

pirocycle (11). Obtained as a thick pale yellow oil by preparative t.l.c. Found: C, 85.15; H, 5.40; N, 4.15. $C_{23}H_{17}NO$ requires 85.40; H, 5.30; , 4.35%); δ 7.97 -6.6 (m,14H,ArH + =CH), 5.81 (d,1H, J 4.5Hz, =CH) and 4.66 nd 4.00 (2xd, 2x1H, J 14.9Hz, NCH_2); m/z(%) 323 (M^+,100), 232(35), 18(74), 189(32) and 91(63); $\nu_{max.}$ 1690, 1500 and 1380 cm^{-1}.

pirocycles (12a) and (13a). The mixture of isomers crystallised from ether-etroleum ether as colourless prisms, m.p. 119-122°C. [Found (mixed isomers , 85.15; H, 5.65; N, 4.10. $C_{24}H_{19}NO$ requires C, 85.45; H, 5.70; , 4.15%]; m/z(%)(mixed isomers) 337 (M^+,94), 309(24), 246(45), 231(82), 06(100) and 91(31).

12a) δ 7.9-6.6 (m,13H,ArH), 6.2 (m,1H,$CH_2\underline{CH}$=CH), 5.2 (d,1H,CH_2CH=$\underline{CH}$), .7 and 4.1 (2xd, 2x1H, J 15.7Hz, NCH_2) and 3.58 (br s, 2H, CH_2).

13a) δ 7.9-6.6 (m,14H,ArH + ArCH), 5.8 (m,1H,ArCH=$\underline{CH}$), 5.16 and 4.06 2xd, 2x1H, J 15.8Hz, NCH_2) and 2.62 (d,2H, J 3.3Hz, CH_2).

pirocycles (8f), (9b) and N-(cyclohex-1-enyl)-4-methylquinolin-1-one 15a). Preparative t.l.c. (SiO_2) eluting with ether-petroleum ether fforded two fractions as pale yellow oils. One consisted of a 1:1 mixture f (8f) and (9b) whilst the other was (15a).

8f) δ 7.8-7.3 (m,4H,ArH), 6.2 (m,1H, ring vinyl-H), 6.0 (m,1H, $\underline{CH}$=CH_2), .23-5.14 (3xd, 3H, CH=$\underline{CH_2}$ and ring vinyl-H), 4.3 (m,2H,NCH_2) and 2.8-.5 (m,6H,3xCH_2).

9b) δ 7.8-7.3 (m,4H,ArH), 6.0 (m,3H,$\underline{CH}$=CH_2 and 2 x ring vinyl -H), 5.23 nd 5.14 (2xd, 2x1H, CH=$\underline{CH_2}$), 4.2 (m,2H,NCH_2) and 2.8-1.5 (m,6H,3xCH_2). /z(%) (8f + 9b) 239 (M^+,32), 185(100) and 170(22); accurate mass 8f+9b): 39.1313. $C_{16}H_{17}NO$ requires 239.1310.

15a) Accurate mass: 239.1324. $C_{16}H_{17}NO$ requires 239.1310. δ 8.4-7.2 m,4H,ArH), 6.87 (s,1H,NCH), 5.8 (m,1H, ring vinyl -H), 2.4-1.62 (m, 6H, x CH_2) and 2.27 (s,3H,Me); m/z(%) 239 (M^+,100), 224(8), 185(46) and 70(12).

-(3,3,5,5-Tetramethylcyclohex-1-enyl)-4-methylquinolin-1-one (15b). btained as thick pale yellow oil by preparative t.l.c. (SiO_2) eluting ith 3:7 v/v petroleum ether-ether (Found: C, 78.20; H, 8.05; N, 4.95.

$C_{20}H_{25}NO$. 0.75 H_2O requires C, 78.15; H, 8.10; N, 4.55%); δ 8.49-7.27 (m,4H,ArH), 6.83 and 5.53 (2xs, 2x1H, =CH), 2.28 (s,3H,Me), 2.19 and 1.44 (2 2 x s, 2 x 2H, 2 x CH_2), and 1.42 and 1.11 (2 x s, 2 x 6H, 4 x Me); m/z(%) 295 (M^+,100), 280(79) and 159(29); $\nu_{max.}$ 1660, 1490 and 1370 cm^{-1}

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