Tetrahedron Vol. 48, No. 44, pp. 9735-9744, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

X=Y–ZH Systems as Potential 1,3-Dipoles. Part 36.[1] 1,5-Electrocyclisation Processes via Oxidation of Tertiary Amines. Pyrrolo-dihydroisoquinolines and -dihydro-β-carbolines.

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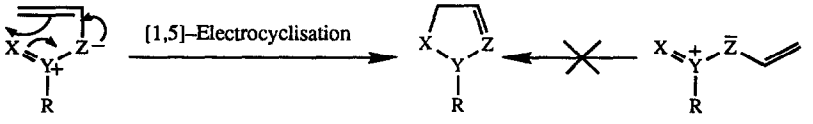
(*Received in UK* 20 *June* 1992)

Key Words: Silver (I) oxidation, azomethine ylides, electrocyclisation.

Abstract. *A range of tertiary N–allylamines derived from 1,2,3,4–tetrahydroisoquinoline undergo oxidative cyclisation, induced by Ag_2CO_3, to pyrrolo–dihydroisoquinolines in moderate to good yield. Analogous oxidative cyclisations are reported for N–allyl–tetrahydro–β–carbolines and a pyrrolidine. The reactions proceed via formation of a 1,5–dipole followed by an electrocyclisation and subsequent aromatisation.*

When a 1,3–dipole is conjugated to a double bond or a 1,3–diene moiety (homo– or hetero–polar) an intramolecular process, 1,5– or 1,7– electrocyclisation, may occur provided the reactive intermediate has the required configuration e.g. Scheme 1.

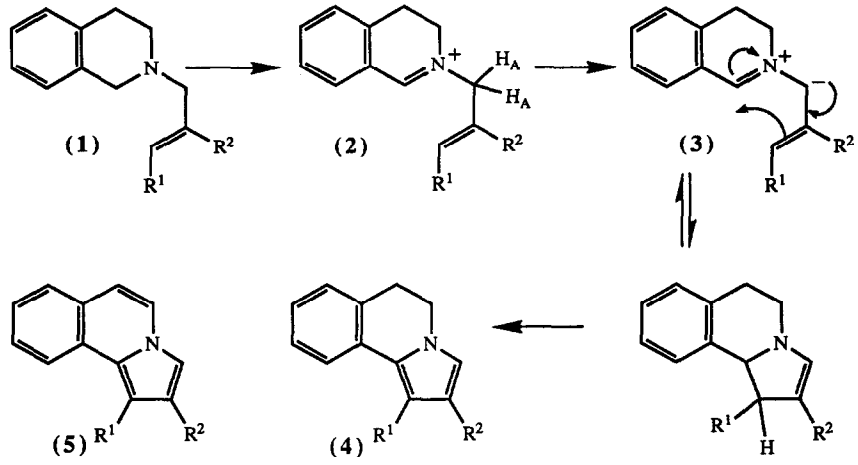


Scheme 1

The stereochemistry of electrocyclic processes was rationalised by Woodward and Hoffmann in terms of the symmetry of the HOMO (for themal processes),[2] although relatively little is known about the factors which influence the rate of cyclisation. 1,5–Electrocyclisation and the corresponding ring–opening processes have attracted most attention.[3] As well as 1,5–electrocyclisations involving 1,5–dipoles,[4,5] the electrocyclisation of the corresponding anionic[6] and cationic[7] species are also known. The electrocyclic ring closure requires a U configuration of the open–chain reactive intermediate although W and S configurations may often be more stable and in charged, as opposed to dipolar species, the configuration is sensitive to the counterion.[8]

Our interest in 1,5–electrocyclisation reactions arises from our ongoing program of devising simple new methods for generating 1,3–dipoles.[9] As part of this program we reported 1,5–electrocylisations of vinyl azomethine ylides generated by 1,2–prototropy from imines and by deprotonation of vinyl iminium species.[10] We have also recently shown that both azomethine ylides[11]

and azomethine imines[12] can be generated regio– and stereo–specifically by catalytic dehydrogenation of tertiary amines and 1,1,2–trisubstituted hydrazines respectively using metal blacks and Wilkinson's catalyst. It was therefore of interest to see if we could generate 1,5–dipoles by dehydrogenation or oxidation and achieve a subsequent 1,5–electrocyclisation. The initial substrates selected for the study were the N–allyltetrahydroisoquinolines (1a–f). Attempts to effect catalytic dehydrogenation of (1) to the iminium species (2), and thence the 1,5–dipoles (3) (Scheme 2) by deprotonation, with Pd black, Ru black and Wilkinson's catalyst were unsuccessful. In search of an oxidant to effect the desired iminium ion formation we turned next to silver carbonate. Silver carbonate on celite is known to oxidise hydroxylamines to nitrones,[13] primary aromatic amines to nitro compounds,[14] and to dehydrogenate alcohols.[15]



Scheme 2

Table 1. Oxidative cyclisation of (1a–f) with Ag_2CO_3[a]

Substrate (1)	Solvent	Temp (°C)	Time (h)	Yield (%)	Product Ratio (4) : (5)
a) $R^1 = R^2 = H$	Toluene	110	18	42	1 : 0
b) R^1 = Ph, R^2 = H	Xylene	140	50	56	1 : 0
c) R^1 = Me, R^2 = H	Xylene	140	24	50	1.3 : 1
d) R^1 = H, R^2 = Me	Xylene	140	40	46	1.2 : 1
e) $R^1 = CO_2Me$, R^2 = H	Xylene	140	16	67	2.5 : 1
	Toluene	110	22	70	2.3 : 1
f) R^1 = H, $R^2 = CO_2Me$	Xylene	140	24	58	1 : 1

a. All reactions employed an excess of Ag_2CO_3 (2.5 mol) and metallic silver is deposited during the reaction.

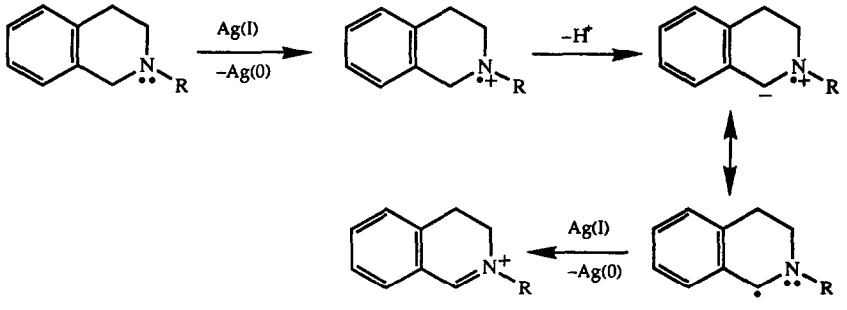
When the N–allyltetrahydroisoquinolines were heated in toluene or xylene containing silver carbonate (2.5 mol) they afforded the pyrrolo–dihydroisoquinolines (4) together with, in most cases,

the corresponding isoquinolines (5) arising from further oxidation. Isolation and characterisation of these pyrroles was somewhat laborious due to their instability. The electron rich pyrroles with electron donating substituents undergo cycloaddition with molecular oxygen (air) and other oxidative processes leading to decomposition.

The structure of the pyrroles (4a–f) and (5c–f) were assigned on the basis of their pmr and mass spectral data. The pyrrole protons appeared as characteristic doublets or singlets between δ 5.9–6.5 with a small coupling constant of 2.3 Hz for the former. All ring protons of (5c–f) resonate in the aromatic region.

Location of conjugating substituents at the allyl terminus, (1b) and (1e), results in a faster reaction and an improved yield of products. In a multistep process such as that outlined in Scheme 2 the role of substituents is not immediately obvious. However, the pKa of the protons H_A in (2b) and (2e) should be substantially lower than the analogous protons of the other iminium ions (2a), (2b), (2d) and (2f). Thus, dipole.formation may be slow step in the sequence whilst oxidation of the dihydropyrrole to the pyrrole in toluene or xylene at 110–140°C is apparently fast.[10]

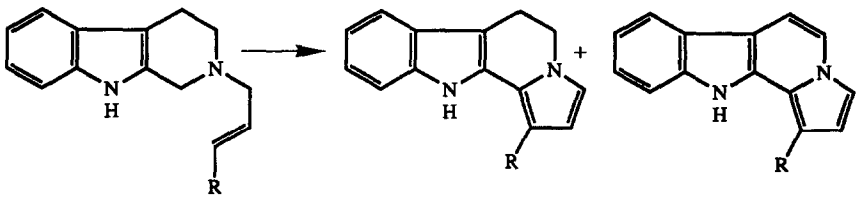
The conversion of the tertiary amine to the corresponding iminium ion presumably proceeds via the tertiary amine radical cation as outlined in Scheme 3. Such species are known to have exceptionally weak C–H bonds.[16] Moreover, the pKa of the C–H protons is *ca.* 11.[17] The mechanism suggested in Scheme 3 indicates the possiblity of cyclisation involving either the mesomeric radical intermediate or the iminium ion itself. However, the substituent effects apparent from Table 1 militate against the former species participating in the cyclisation step.



Scheme 3

The most promising substitution in (1) was applied to the tetrahydro–β–carboline series and the N–allyl derivatives (6a) and (6b) were prepared. Attempted oxidative cyclisation with silver carbonate in boiling xylene was disappointing with (6b) undergoing slow decomposition with no discernible formation of the product whilst (6a) gave a low yield (33%) of a 2 : 1 mixture of (7a) and (8a). The π–excessive character of the indole nucleus is thus exerting a deleterious effect on the process.

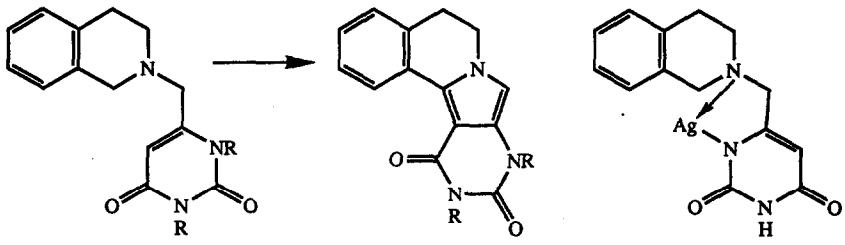
Attempts to oxidatively cyclise the pyrimidinyl derivative (9a) with silver carbonate (xylene, 140 °C) were unsuccessful, with (9a) being recovered largely unchanged. The failure of (9a) to cyclise may be due to formation of a stable Ag(I) chelate complex (11) and this suggested a study of the corresponding N,N–dimethyl derivative (9b). In this case a slow cyclisation (xylene, 140 °C) did occur but had proceeded to only 50% conversion after 50 h. The product (10b)was obtained in 42% yield.



(6)a. R = CO_2Me
b. R = Ph

(7)a. R = CO_2Me
b. R = Ph

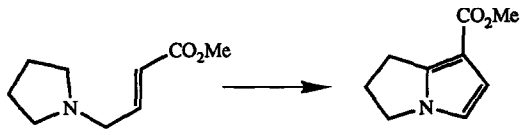
(8)a. R = CO_2Me
b. R = Ph



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

(10)

(11)



(12)

(13)

One example, (12), of non–benzylic tertiary amine was studied. The reaction (xylene, 140 °C) was slow and had proceeded to 50% conversion (pmr) after 48h when work up afforded the bicyclic pyrrole (13) (30%).

All successful oxidative cyclisation processes were carried out in non–polar solvents. Reactions in DMF (120–130 °C) resulted in intractable mixtures.

Experimental

General experimental details were as previously described.[1]

General procedure for the synthesis of tertiary amine precursors.

Amine (25mmol), alkyl halide (25mmol) and anhydrous potassium carbonate (30mmol) were mixed in dry CH_3CN (40–50 ml) and stirred at room temperature for 18–20 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was purified by distillation (reduced pressure) or chromatography to afford the *product*.

N–Allyl–1,2,3,4–tetrahydroisoquinoline (1a). Prepared from tetrahydroisoquinoline (2.5g, 18.8mmol) and allyl bromide (2.3g, 18.8mmol) with K_2CO_3 (3.0g, 22.0mmol) in CH_3CN (40ml), stirring at room temperature for 5 h. Column chromatography eluting with 92 : 8 v/v ether–methanol

afforded the *product* as a yellow thick oil (1.7g, 53%). A portion of the oil was molecularly distilled to afford a colourless liquid, b.p. 80–82 °C (furnace temp.)/0.08mmHg. (Found: C, 83.15; H,8.8; N, 8.25 $C_{11}H_{15}N$ requires : C, 83.25; H, 8.65; N, 8.1%) δ 7.20–6.95 (m, 4H, ArH), 6.08–5.91 (m, 1H, $NCH_2\underline{CH}$=), 5.35–5.19 (m, 2H, CH=$\underline{CH_2}$), 3.64 (s, 2H, $ArCH_2N$), 3.19 (d, 2H, J 6.36 Hz, $N\underline{CH_2}CH$=), 2.92 (t, 2H, $Ar\underline{CH_2}CH_2N$) and 2.72 (t, 2H, $ArCH_2\underline{CH_2}N$); m/z(%) 173 (M^+, 60), 172 (100), 146 (24), 131 (15), 104 (56) and 40 (57).

N–Cinnamyl–1,2,3,4–tetrahydroisoquinoline (1b). Prepared from tetrahydroisoquinoline (3.0g, 23.0mmol) and cinnamyl bromide (4.44g, 23.0mmol) with K_2CO_3 (3.8g, 28.0mmol) in dry CH_3CN (40ml) over 10 h. Column chromatography eluting with ether afforded the *product* as a yellow semi–solid (2.9g, 52%) which solidified upon standing in the freezer. Crystallisation from ether afforded yellow plates, m.p. 43–45 °C. (Found : C, 86.65; H, 7.8; N, 5.5 $C_{18}H_{19}N$ requires : C, 86.75; H, 7.65; N, 5.6 %). δ 7.50–7.04 (m, 9H, ArH), 6.59 (d, 1H, J 15.93 Hz, $NCH_2CH=\underline{CH}$), 6.46 (m, 1H $CH_2\underline{CH}$=C), 3.67 (s, 2H, $ArCH_2N$), 3.32 (d, 2H, J 6.74 Hz, $N\underline{CH_2}$ CH), 2.93 (t, 2H, $Ar\underline{CH_2}CH_2N$) and 2.79 (t, 2H, $ArCH_2\underline{CH_2}N$); m/z(%): 249 (M^+, 29), 172 (4), 159 (15), 146 (26), 132 (63), 117 (100), 104 (81) 91 (61) and 77 (35).

N–Crotyl–1,2,3,4–tetrahydroisoquinoline (1c). Prepared from tetrahydroisoquinoline (5g, 37.6mmol) and crotyl bromide (5.1g, 37.6mmol) with K_2CO_3 (6.1g, 44.2mmol) in CH_3CN (50ml), over 18 h. Distillation under reduced pressure afforded the *product* as a yellow oil (3.2g, 46%), b.p. 86-87 °C/0.5mmHg. (Found : C, 83.25, H, 9.25, N, 7.6. $C_{13}H_{17}N$ requires : C, 83.4, H, 9.1, N, 7.5 %); δ 7.07-6.98 (m, 4H, ArH), 5.61 (m, 2H, $\underline{CH=CH}CH_3$), 3.59 and 3,56 (s, 2H, $ArCH_2N$), 3.15 and 3.05 (d, 2H, J 6.46 and 5.37 Hz, $N\underline{CH_2}CH$=), 2.86 (t, 2H, $Ar\underline{CH_2}CH_2N$), 2.67 (t, 2H, $ArCH_2\underline{CH_2}N$) and 1.69 and 1.23 (2xd, 3H, J 5.69 and 6.60 Hz, Me); m/z(%) 187 (M^+, 50), 186 (100), 146 (49), 132 (84), 104 (81) and 77 (19).

N–(2–Methylprop–2–enyl)–1,2,3,4–tetrahydroisoquinoline (1d). Prepared from 1,2,3,4–tetrahydroisoquinoline (5g, 37.5mmol) and methallyl chloride (3.4g, 37.5mmol) with K_2CO_3 (6.2g, 45.0mmol) in CH_3CN (60ml), over 16 h. The *product* distilled as a yellow oil (4.8g, 69%), b.p. 66-68 °C/0.15mmHg. (Found : C, 83.0; H, 9.1; N, 7.5. $C_{13}H_{17}N$ requires : C, 83.5; H, 9.1; N, 7.5%); δ 7.11-7.0 (m, 4H, ArH), 4.91 (d, 2H, J 13.5 Hz, $\underline{CH_2}$=C), 3.56 (s, 2H, $ArCH_2N$), 3.04 (s, 2H, $N\underline{CH_2}CH$=), 2.88 (t, 2H, $Ar\underline{CH_2}CH_2N$), 2.65 (t, 2H, $ArCH_2\underline{CH_2}N$), and 1.79 (s, 3H, Me); m/z(%) 183 (M^+, 100), 168 (14), 146 (6), 119 (8), 105 (8) and 91 (12).

N–(3–Carbomethoxyprop–2–enyl)–1,2,3,4–tetrahydroisoquinoline (1e). Prepared from 1,2,3,4–tetrahydroisoquinoline (3.7g, 27.8mmol), and methyl–4– bromocrotonate (5g, 27.8mmol) with K_2CO_3 (5.8g, 42.0mmol) in CH_3CN (50ml), over 18 h. The *product* distilled as a yellow oil (5.1g, 80%), b.p. 84-86 °C/0.5mmHg. (Found : C, 72.4; H, 7.5; N, 6.35. $C_{14}H_{17}NO_2$ requires : C, 72.7; H, 7.4; N, 6.1 %); δ 7.14 -7.08 (m, 3H, ArH), 6.97 (m, 2H, ArH and $NCH_2\underline{CH}$=CH), 6.06 (d, 1H, J 15.82 Hz, $NCH_2CH=\underline{CH}$), 3.74 (s, 3H, CO_2Me), 3.63 (s, 2H, $Ar\underline{CH_2}N$), 3.30 (d, 2H, J 6.21 Hz, NCH_2), 2.90 (t, 2H, $Ar\underline{CH_2}CH_2N$) and 2.73 (t, 2H, $ArCH_2\underline{CH_2}N$); m/z(%) 231 (M^+, 69), 216 (44), 172 (33), 146 (32), 104 (100), 77 (25) and 59 (8).

N–(2–Methoxycarbonylprop–2–enyl)–1,2,3,4–tetrahydroisoquinoline (1f). Prepared from 1,2,3,4–tetrahydroisoquinoline (2.23g, 16.8mmol) and methyl α–bromomethylacrylate (3.0g, 16.8mmol) and K_2CO_3 (2.8g, 20.2mmol), in CH_3CN (50ml), over 18 h. Column chromatography eluting with ether afforded a yellow oil (3.7g, 97%), a small portion of which was molecularly

distilled, b.p. 98-102 °C (furnace temperature) /0.2mmHg. (Found : C, 72.4; H, 7.2; N, 6.4. $C_{14}H_{17}NO_2$ requires : C, 72.7; H, 7.4; N, 6.1 %); δ 7.27-7.10 (m, 4H, ArH), 6.34 (s, 1H, cis–CH=CCO), 5.88 (s, 1H, trans–CH=CCO), 3.78 (s, 3H, CO_2Me), 3.69 (s, 2H, $ArCH_2N$), 3.41 (s, 2H, NCH_2C=), 2.91 (t, 2H, $ArCH_2CH_2N$), and 2.79 (t, 2H, $ArCH_2CH_2N$); m/z(%) 231 (M^+, 2), 216 (24), 172 (2), 146 (22), 13 (100), 105 (13) and 91 (13).

N–(3–Methoxylcarbonylprop–2–enyl)–1,2,3,4–tetrahydropyrido[3,4–*b*]indole (6a). Prepared from tetrahydro-β-carboline (1.0g, 5.8mmol) and methyl 4-bromocrotonate (1.03g, 5.8mmol), with K_2CO_3 (1.0g, 7.0mmol) in CH_3CN (40ml), over 20 h. Flash chromatography eluting with ether afforded the *product* as a yellow solid (0.95g, 60%), which crystallised from ether as yellow needles, m.p. 165–167 °C. (Found : C, 70.0; H, 6.60; N,10.25. $C_{16}H_{18}N_2O_2 \cdot 0.2H_2O$ requires : C, 70.1; H, 6.55; N, 10.25 %); δ 7.89 (br s, 1H, NH), 7.46 (d, 1H, J 7.09 Hz, ArH), 7.26 (d, 1H, ArH), 7.25-7.02 (m, 3H, ArH and CH=CHCO) , 6.06 (d, 1H, J 15.73 Hz CH=CHCO), 3.76 (s, 3H, CO_2Me), 3.62 (s, 2H, $ArCH_2N$), 3.35 (d, 2H, J 6.01 Hz, NCH_2), 2.85 (t, 2H, J 4.57 Hz, $ArCH_2CH_2N$), and 2.81 (t, 2H, J 4.75 Hz, $ArCH_2CH_2N$); m/z(%) 270 (M^+, 7), 210 (5), 171 (23), 142 (100) and 114 (19).

N–Cinnamyl–1,2,3,4–tetrahydro–9H–pyrido[4,5–*b*]indole (6b). Prepared from 1,2,3,4–tetrahydro–β–carboline (1.0g, 5.8mmol) and cinnamyl bromide (1.15g, 5.8mmol) with K_2CO_3 (0.96g, 7.0mmol) in CH_3CN (35ml), over 18 h. The *product* (0.9g, 54%) crystallised from ether as yellow rods, m.p. 154–155 °C. (Found : C, 83.2; H, 6.95; N, 9.5. $C_{20}H_{20}N_2$ requires : C, 83.35; H, 6.95; N, 9.7 %); δ 8.14 (br s, 1H, NH), 7.55–7.19 (m, 9H, ArH), 6.73 (d, 1H, J 15.9 Hz, NCH_2CH=CH), 6.48 (m, 1H, NCH_2CH=CH), 3.89 (s, 2H, $ArCH_2N$), 3.56 (d, 2H, NCH_2CH=CH), 3.08 (t, 2H, $ArCH_2CH_2N$) and 2.99 (t, 2H, $ArCH_2CH_2N$); m/z(%) 288 (M^+, 7), 184 (4), 157 (3), 143 (100), 129 (2), 115 (16), 91 (18) and 77 (6).

2–(2,4–Dioxopyrimidyl)methyl–1,2,3,4–tetrahydroisoquinoline (9a). Prepared from tetrahydroisoquinoline (1.0g, 7.5mmol) and 6–(chloromethyl) uracil (1.2g, 7.5mmol) with K_2CO_3 (1.24g, 9.0mmol), in CH_3CN (50 ml), over 16 h. The solvent was removed and the residue was extracted with CH_2Cl_2 using a soxhlet apparatus (overnight). The resulting yellow solid, was purified by flash chromatography eluting with 9 : 1 v/v ether–methanol to afford the *product* as colourless rods from methanol (0.75g, 39%), m.p. 239–241 °C. (Found : C, 65.3;H, 5.95; N, 16.6. $C_{14}H_{15}N_3O_2$ requires : C, 65.35; H, 5.85; N, 16.35 %); δ 8.62 (br s, 2x 1H, 2x NH), 7.17-7.15 (m, 3H, ArH), 7.00 (d, 1H, J 7.2 Hz, ArH), 5.61 (s, 1H, CH=), 3.69 (s, 2H, $ArCH_2N$), 3.50 (s, 2H, NCH_2C=), 2.95 (t, 2H, $ArCH_2CH_2N$) and 2.83 (t, 2H, $ArCH_2CH_2N$). m/z(%) 257 (M^+, 6), 132 (100), 126 (8), 111 (5), 105 (18), 91 (11) and 77 (16).

N–(1,3–Dimethyl–2,4–dioxopyrimidyl)methyl–1,2,3,4–tetrahydroisoquinoline (9b). Amine (9a) (0.5g, 2.0mmol) was added to a stirred solution of tetraethylammonium fluoride hydrate (1.5g) in dry THF (50 ml), and stirred at room temperature. Methyl iodide (0.85g, 6.0mmol) was added to the resulting suspension, which was stirred for a further 20 h, at which time the mixture comprised a yellow solution with a white precipitate. The white precipitate was filtered and the filtrate was evaporated under reduced pressure to leave a yellow solid, which was purified by column chromatography eluting with 9 : 1 v/v ether–methanol to afford the *product* as a pale yellow solid (0.45g, 82%), which crystallised from ether as colourless needles, m.p. 111–112 °C. (Found : C, 67.25; H, 6.8; N, 14.5. $C_{16}H_{19}N_3O_4$ requires : C, 67.35; H,6.65; N,14.75 %); δ 7.14 (m, 4H,

ArH), 7.02 (m, 1H, ArH), 5.79 (s, 1H, CH=), 3.69 (s, 2H, $ArCH_2N$), 3.53 (s, 3H, NMe), 3.44 (s, 2H, NCH_2C=), 3.35 (s, 3H, NMe), 2.91 (m, 2H, $ArCH_2CH_2N$), and 2.81 (m, 2H, $ArCH_2CH_2N$); m/z(%) 285 (M^+, 2), 146 (19), 154 (16), 132 (100), 104 (34) and 91 (9).

2–(3–Methoxycarbonylprop–2–enyl)pyrrolidine (12). Prepared from pyrrolidine (1g, 14.0mmol) and methyl 4– bromocrotonate (2.5g, 14.0mmol) with K_2CO_3 (2.4g, 17.4mmol) in CH_3CN (30ml), over 18 h. Flash chromatography eluting with ether afforded the *product* as a yellow oil(0.63g, 30%). Found(H.R.M.S) : 169.10945. $C_9H_{15}NO_2$ requires : 169.11027; δ 6.93 (m, 1H, NCH_2CH=), 5.89 (d, 1H, J 15.72 Hz, NCH_2CH=CH), 3.63 (s, 3H, CO_2Me), 3.14 (d, 2H, J 4.46 Hz, NCH_2CH=), 2.42 (br s, 2x2H, 2xNCH_2CH_2) and 1.69 (brs, 2x 2H, 2x NCH_2CH_2); m/z(%) 169 (M^+, 23), 168 (100), 154 (18), 138 (6) 110 (33), 97 (42), 84 (53) and 70 (40).

General procedure for the silver carbonate promoted cyclisation reactions.

Tertiary amine (25mmol) and silver carbonate (62.5mmol) were mixed in dry toluene or xylene (25ml) and boiled under reflux for 18-48 h. The reaction mixture was cooled to room temperature and the solvent was evaporated *in vacuo* to give a dark coloured residue. The residue was dissolved in CH_2Cl_2 (40ml), filtered through a celite pad and the solvent evaporated to leave a dark coloured liquid or solid, which was purified by column chromatography.

5,6–Dihydrobenzo[*g*]indolizine (4a). A mixture of N–allyl–1,2,3,4–tetrahydroisoquinoline (0.5g, 3.0mmol) and Ag_2CO_3 (2.4g, 9.0mmol) heated under reflux in xylene (25ml) for 50 h. Column chromatography eluting with 3 : 1 v/v ether–petroleum ether afforded the *product* (0.25g, 42%) as a thick yellow oil. The same reaction when performed in boiling toluene 50 h, showed 50% conversion of the starting material (31% yield). Found (H.R.M.S) : 169.08920. $C_{12}H_{11}N$ requires : 169.08915; δ 7.52–7.07 (m, 4H, ArH), 6.67 (t, 1H, pyrrole–H), 6.50 (d, 1H, J 3,40 Hz, pyrrole–H), 6.21 (d, 1H, J 2.53 Hz, pyrrole–H), 4.08 (t, 2H, $ArCH_2CH_2N$) 3.06 (t, 2H, $ArCH_2CH_2N$); m/z(%) 169 (M^+, 29), 115 (3), 88 (1) and 40 (100).

1–Phenyl–5,6–dihydrobenzo[*g*]indolizine (4b). A mixture of N–cinnamyl–1,2,3,4–tetrahydroisoquinoline (0.5g, 2.0mmol) and Ag_2CO_3 (1.38g, 5.0mmol) were heated under reflux in xylene (20ml) for 18 h. Flash chromatography eluting with ether afforded the *product* (0.28g, 57%) which crystallised from ether as colourless prisms, m.p.99–101 °C. (Found : C, 88.0; H, 6.15; N, 5.65. $C_{18}H_{15}N$ requires : C, 88.15; H, 6.1; N, 5.7 %); δ 7.51–7.02 (m, 9H, ArH), 6.72 (d, 1H, J 2.21 Hz, pyrrole–H), 6.24 (d, 1H, J 2.14 Hz, pyrrole–H), 4.06 (t, 2H, $ArCH_2CH_2N$) and 3.09 (t, 2H, $ArCH_2CH_2N$); m/z(%) 245 (M^+, 100), 120 (98), 115 (13) and 77 (11).

1–Methyl–5,6–dihydrobenzo[*g*]indolizine (4c). A mixture of N–crotyl–1,2,3,4–tetrahydroisoquinoline (0.48g, 2.6mmol) and Ag_2CO_3 (1.77g, 6.4mmol) were boiled in xylene (20ml) for 24 h. Column chromatography afforded the *product* (0.23g, 50%) as a yellow oil . The colour of the product changed from yellow to light green and then to dark green upon standing at room temperature. The minor isomer (**5c**) was not isolated. (Found : C, 85.35; H, 7.2; N, 7.4. $C_{18}H_{19}N$ requires : C, 85.24; H, 7.1; N, 7.65 %); δ 7.50 (d, 1H, J 7.74 Hz, ArH), 7.18-7.0 (m, 3H, ArH), 6.49 (d, 1H, J 2.36 Hz, pyrrole–H), 5.96 (d, 1H, J 2.24 Hz, pyrrole–H), 3.95 (t, 2H, $ArCH_2CH_2N$), 2.94 (t, 2H, $ArCH_2CH_2N$) and 2.32 (s, 3H, Me); m/z(%) 183 (M^+, 100), 168 (11), 149 (23), 105 (17) and 91 (6).

2–Methyl–5,6–dihydrobenzo[g]indolizine (4d) and 2–Methylbenzo[g]indolizine (5d). A mixture of N–(2–methylprop–2–enyl)–1,2,3,4-tetrahydroisoquinoline (0.5g, 2.7mmol) and Ag_2CO_3 (1.8g, 6.7mmol) were heated under reflux in xylene (15ml) for 40 h, when the pmr spectrum of the reaction mixture showed 75% conversion of the starting material. Flash chromatography eluting with CH_2Cl_2 to afforded the *products* (0.17g, 46%), which were further separated by flash chromatography eluting with petroleum ether.

(4d) Semi–solid at room temperature which formed colourless needles at 0 °C. (Found : C, 85.1; H, 7.2; N, 7.75. $C_{13}H_{13}N$ requires : C, 85.2; H, 7.1; N,7.65%) δ 7.43 (d, 1H, J 7.69 Hz, ArH), 7.17-7.03 (m, 3H, ArH), 6.43 (s, 1H, pyrrole–H), 6.34 (s, 1H, pyrrole–H), 3.97 (t, 2H, Ar$\underline{CH_2}CH_2N$), 3.01 (t, 2H, $ArCH_2\underline{CH_2}N$) and 2.13 (s, 3H, Me); m/z(%) 183 (M^+, 100), 168 (14), 146 (6), 119 (8), 105 (8) and 91 (12).

(5d) Crystallised from ether–petroleum ether as colourless needles, m.p. 94-96 °C. (Found : C, 86.1; H, 6.25; N, 7.55. $C_{13}H_{11}N$ requires : C, 86.2; H, 6.1; N, 7.75 %); δ 7.90 (d, 1H, J 8.11Hz, ArH), 7.53 (d, 1H, J 7.23 Hz, ArH), 7.47 (s, 1H, NCH=C), 7.36 (t, 1H, ArH), 7.25 (t, 1H, ArH), 6.98 (s, 1H, =CCH=C), 6.56 (d, 1H, J 7.32Hz, ArH) and 2.30 (s, 3H, Me); m/z(%) 181 (M^+, 29), 166, (9), 153 (7), 141 (5), 127 (7) and 90 (11).

1–Methoxycarbonyl–5,6–dihydrobenzo[g]indolizine (4e) and 1–Methoxycarbonyl benzo[g]indolizine (5e). Carbomethoxyprop–2–enyl–1,2,3,4–tetrahydroisoquinoline (0.9g, 3.9mmol) and Ag_2CO_3 (2.7g, 9.7mmol) were boiled under reflux in xylene (30ml) for 18 h. Column chromatography eluting with CH_2Cl_2 afforded the *products* **(4e)** (0.49g, 56%) and **(5e)** (0.1g, 11.5%) as colourless solids.

When the reaction was repeated in boiling toluene the combined products were obtained in 70% yield.

(4e) Crystallised from ether as colourless rods, m.p. 75–77 °C. (Found : C, 74.15; H, 5.85; N, 5.95. $C_{14}H_{17}NO_2$ requires : C, 74.0; H, 5.7; N, 6.2 %); δ 8.53 (d, 1H, J 7.98 Hz, ArH), 7.35-7.21 (m, 3H, ArH), 6.70 (d, 1H, J 2.89 Hz, NCH=$\underline{CH}$), 6.63 (d, 1H, J 2.92 Hz, NCH=$\underline{CH}$), 4.05 (t, 2H, Ar$\underline{CH_2}CH_2N$), 3.85 (s, 3H, CO_2Me) and 3.04 (t, 2H, $ArCH_2\underline{CH_2}N$); m/z(%) 227 (M^+, 96), 212 (4), 196 (100), 167 (41), 139 (37), 105 (9), 91 (3) and 77 (4).

(5e) Crystallised from ether as colourless rods, m.p. 99-100 °C. (Found : C, 74.85; H, 4.95; N, 6.05. $C_{14}H_{11}NO_2$ requires : C, 74.65; H, 4.9; N, 6.2 %); δ 9.83 (d, 1H, J 8.23 Hz, ArH), 7.78 (d, 1H, J 7.27 Hz, ArH), 7.63-7.51 (m, 4H, ArH), 7.21 (t, 1H, ArH), 6.95 (d, 1H, J 7.16 Hz, ArH), and 3.93 (s, 3H, CO_2Me); m/z(%) 225 (M^+, 85), 194 (100), 166 (24) and 139 (40).

2–Methoxycarbonyl–5,6–dihydrobenzo[g]indolizine (4f) and 2–Methoxycarbonyl benzo[g]indolizine (5f). A mixture of 2–methoxycarbonylprop–2–enyl– 1,2,3,4– tetrahydroiso–quinoline(0.27g, 1.2mmol) and Ag_2CO_3 (0.81g, 3.0mmol) was boiled under reflux in xylene (20ml) for 24 h. Preparative t.l.c eluting with CH_2Cl_2 afforded the *products* (0.15g) in a combined yield of 58%.

(4f) Obtained as a colourless semi–solid. (Found : C, 73.9; H, 5.85; N, 6.35. $C_{14}H_{13}NO_2$ requires : C, 74.0; H, 5.75; N, 6.9 %); δ 7.53 (d, 1H, J 7.54 Hz, ArH), 7.31-7.16 (m, 4H, ArH), 6.91 (s, 1H, NCH=C$\underline{CH}$=), 4.11 (t, 2H, Ar$\underline{CH_2}CH_2N$), 3.83 (s, 3H, CO_2Me), and 3.08 (t, 2H, $ArCH_2\underline{CH_2}N$); m/z(%) 227 (M^+, 79), 196 (100), 168 (25), 139 (21), 119 (4), 105 (12), 91 (8) and 77 (13).

(5f) Obtained as a colourless semi–solid. Found (H.R.M.S) : 225.0794. $C_{14}H_{11}NO_2$ requires :

225.0790; δ 7.52 (d, 1H, J 7.53 Hz, ArH), 7.41–7.22 (m, 6H, ArH), 6.81 (s, 1H, NCHCCH) and 3.68 (s, 3H, CO_2Me); m/z(%) 225 (M^+, 16), 166 (16), 141 (12), 132 (19), 128 (31), 105 (100) and 59 (6).

1–Methoxycarbonyl–2,3–dihydroindolizidino[4,5-*b*]indole (7a) and 1–Methoxycarbonylindolizidino[4,5-*b*]indole(8a). A mixture of N–3–methoxycarbonylprop–2–enyl–1,2,3,4–tetrahydro pyrido–[3,4–*b*]indole (0.2g, 0.7mmol) and Ag_2CO_3 (0.5g, 0.18mmol) was boiled under reflux in xylene (20ml) for 48 h. The pmr spectrum of the reaction mixture showed only 80% conversion of the starting material. Flash chromatography eluting with CH_2Cl_2 afforded the *products* (0.05g, 33%) as yellow semi–solids.

(7a) Found (H.R.M.S) : 266.105447. $C_{16}H_{14}N_2O_2$ requires : 266.10552; δ 10.87 (br s, 1H, NH), 7.51 (d, 1H, J 7.58 Hz, ArH) 7.42 (d, 1H, J 7.39 Hz, ArH), 7.18 (m, 2H, ArH), 6.64 (d, 1H, J 2.91 Hz, pyrrole–H), 6.56 (d, 1H, J 3.04 Hz, pyrrole–H), 4.19 (t, 2H, J 7.3 Hz, $ArCH_2CH_2N$), 3.88 (s, 3H, CO_2Me) and 3.19 (t, 2H, J 7.31 Hz, $ArCH_2CH_2N$); m/z(%) 266 (M^+, 100), 234 (89), 205 (25) and 178 (22).

(8a) Found (H.R.M.S) : 264.0895. $C_{16}H_{12}N_2O_2$ requires : 264.0898; δ 11.43 (br s, 1H, NH), 7.98 (d, 1H, J 7.83 Hz, ArH), 7.82 (d, 1H, J 7.04 Hz, ArH), 7.62 (d, 1H, J 8.1 Hz, ArH), 7.32 (m, 2H, ArH), 7.15 (d, 1H, J 3.03 Hz, ArH), and 3.97 (s, 3H, CO_2Me); m/z(%) 264 (M^+, 76), 232 (100), 177 (37) and 116 (15).

5,6–Dihydro(1,3–dimethyl–2,4–dioxo)pyrimido[5,6–*a*]benzo[*g*]indolizine (10). A mixture of N–(2,4–dioxopyrimidyl)methyl–1,2,3,4–tetrahydroisoquinoline (0.2g, 0.7mmol) and Ag_2CO_3 (0.48g, 1.7mmol) was boiled under reflux in xylene (20ml) for 43 h. The pmr spectrum of the reaction mixture showed 50% conversion to the product. Preparative t.l.c eluting with 98 : 2 v/v ether–methanol afforded the *product* (0.04g, 42%) as a yellow semi–solid. Found (H.R.M.S) : 281.1159. $C_{16}H_{15}N_3O_2$ requires : 281.1164; δ 9.0 (d, 1H, J 8.13 Hz, ArH), 7.45–7.24 (m, 3H, ArH), 6.38 (s, 1H, pyrrole–H), 4.13 (t, 2H, J 6.9 Hz, $ArCH_2CH_2N$), 3.47 (s, 3H, NMe), 3.42 (s, 3H, NMe) and 3.12 (t, 2H, J 6.84 Hz, $ArCH_2CH_2N$); m/z(%) 281 (M^+, 100), 224 (39), 196 (15), 167 (6), 85 (5) and 57 (9).

7–Methoxycarbonyl–2,3–dihydro–1H–pyrrolizine (13). A mixture of N–(3–methoxycarbonylprop–2–enyl)pyrrolidine (0.4g, 2.4mmol) and Ag_2CO_3 (1.6g, 5.9mmol) was boiled under reflux in xylene for 48 h. The pmr spectrum of the reaction mixture showed 50% conversion to the product. Flash chromatography eluting with 19 : 1 v/v CH_2Cl_2–Et_2O afforded the *product* as a semi–solid (0.55g, 30%). It did not prove possible to crystallise the pyrrole which was characterised by its pmr and mass spectral data and by comparisons with the known ethyl ester derivative.[18] δ 6.61 (d, 1H, J 2.9 Hz, pyrrole–H), 6.54 (d, 1H, 2.9 Hz, pyrrole–H), 3.97 (t, 2H, J 7.24 Hz, CH_2N), 3.79 (s, 3H, CO_2Me), 3.06 (t, 2H, J 7.25 Hz, methylene–H) and 2.53 (m, 2H, methylene–H); m/z(%) 165 (M^+, 54), 150 (55), 135 (10), 134 (77), 106 (28), 78 (10) and 31 (100).

We thank Glaxo Laboratories (Greenford) and Leeds University for support.

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