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Reaction of Electron Rich Alkenes with Anilines and Formaldehyde: Syntheses of Tetrahydroquinolines

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Abstract: A one-pot synthesis has been established of tetrahydroquinolines based upon reaction of aromatic amines and formaldehyde with electron rich alkenes such as styrene, α-methylstyrene, 1-phenylcyclohexene and 3,4-dihydro-2H-pyran. The isolation of alcohols as additional products from reactions conducted in acetonitrile containing trifluoroacetic acid, and the demonstration that these alcohols reacted further under similar reaction conditions to give efficiently cyclised products indicates that the cyclisations reported in this paper are not concerted. The importance is discussed of similar multi-step processes in the catalysed addition of electron rich alkenes to preformed imines.

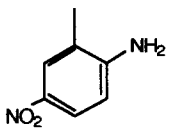
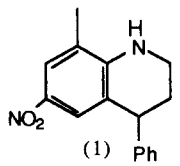
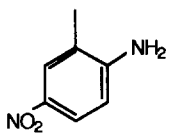
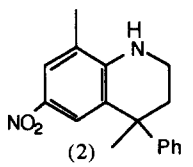
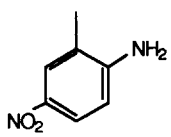
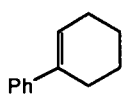
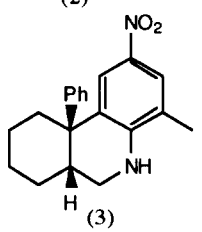
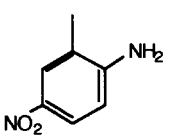
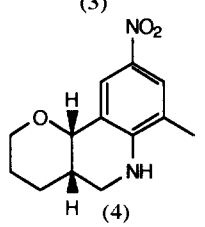
2-Azadienes derived from aromatic primary amines have been used in cycloaddition reactions with electron rich alkenes. These reactions may be considered to be Diels Alder reactions in which the azadiene acts as the electron poor component and the electron rich alkene acts as the dienophile. The azadienes are Schiff 's bases formed from the aromatic amine and an aldehyde. There is an extensive literature concerning these additions. One part, the major part, concerns the reaction of preformed imines[1-4] with alkenes, and another is based on the much less studied reactions of iminium ions or imines, generated *in situ*[5-10], with alkenes. Generally reaction of a neutral imine with an alkene is sluggish, and either iminium ions must be generated under acid conditions or Lewis acids must be used as catalysts. Under acid conditions using preformed imines successful additions can be promoted with a variety of alkene substrates including styrenes, dienes, enol ethers, vinyl sulfides and enamines, and acetylenes. A special valuable application[11] has been the addition of alkenes to the more activated N-acyliminium cations. The major contribution to the study of the reaction of imines generated *in situ* with alkenes is associated with Grieco and Bahsas[6] who devised a one-pot synthesis of tetrahydroquinolines. They described the synthesis of a series of adducts by the addition of imines, generated in the presence of trifluoroacetic acid, to cyclopentadiene. We have subsequently extended this chemistry by reporting[7,8] the addition of cyclopentadiene to aminoanthraquinones, aminoquinolines and aminoisoquinolines. However in view of the limited studies concerning the application of the conditions of Grieco and Bahsas, avoiding prior imine formation, it was interesting to consider the wider possibilities of the synthetic utility of the reaction using other electron rich alkenes with imines generated *in situ*. A further impetus to the study was the appreciation that in most of the reactions reported concerning the formal Diels Alder addition of imines, or iminium ions, to electron rich

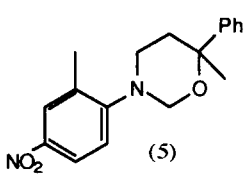
dienophiles, there is little mechanistic evidence to distinguish between concerted and multi-step additions. Here we report a study of the reaction of imines generated *in situ* with a range of electron rich alkenes. These results both greatly extend the synthetic utility of the Grieco and Bahsas[6] conditions, and establish the multi-step nature of the additions, which are not concerted Diels Alder reactions.

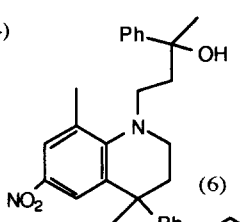
A difficulty observed in studies of cyclocondensation of cyclopentadiene with formaldehyde and anilines is the tendency for initially formed products to undergo a second condensation. Hence in our initial studies we chose to investigate the potential of reactions involving other electron rich alkenes with 2-methyl-4-nitroaniline. This amine has two advantages: the second potential condensation is blocked by the methyl group and an iminium ion derived from this amine is further activated by the nitro group. Reaction of 2-methyl-4-nitroaniline with formaldehyde and styrene in acetonitrile in the presence of trifluoroacetic acid at reflux afforded the cyclocondensation product (1) in 90% yield. At lower temperatures salts of the amine precipitated from the reaction mixture. Spectroscopic observations readily established the assigned structure. Under these reaction conditions no other products were formed in significant amounts. The course of other reactions involving 2-methyl-4-nitroaniline are shown in Table 1, where the major products from reaction of α-methylstyrene, 1-phenylcyclohexene and 3,4-dihydro-2*H*-pyran are the adducts (2-4). Although these adducts can be obtained under the appropriate conditions (see experimental) in 60-80% yields, a number of features complicate the course of reaction. In the case of 3,4-dihydro-2*H*-pyran no side products were observed and the single adduct (4) was isolated. The stereochemistry of this product (4) was defined by observation of the small coupling constant (J 1.8Hz) associated with the ring junction proton C<u>H</u>-O at 4.46ppm. In related *cis* compounds[2,12,13] a similar small coupling has been observed in contrast to a larger coupling (8.8Hz) found[13] in an appropriate *trans* model compound. However under less forcing reaction conditions α-methylstyrene, in addition to formation of the adduct (2) (60%), gave the 1,3-oxazine (5) (24% yield), a diastereoisomeric mixture (6) by further reaction at nitrogen and the intermediate amino-alcohol (7). Each of these minor products was isolated separately and structures were assigned from the appropriate analytical and spectroscopic data. The 1,3-oxazine structure (5) was particularly defined by observation of two doublets (J 11.4Hz) at 4.82 and 4.72ppm associated with the NCH_2O moiety. The minor product (6) (5%) was defined *inter alia* by mass spectral data, observation of the hydroxyl group in the IR spectrum and the absence of an NH signal in the IR spectrum. The amino-alcohol structure (7) was defined by observation of the hydroxyl group in the IR spectrum. The unwanted 1,3-oxazine arises from reaction with excess formaldehyde. Reaction under different conditions permits the isolation of the bicyclic amine (2) in 72% yield with only the alcohol (7) (27%) as a significant side product. Similarly the formation of the product (6) of further reaction clearly arises from presence of excess formaldehyde. Again by appropriate choice of conditions this side product can be avoided. However the most interesting of these products is the amino-alcohol (7). In a number of examples described below similar intermediate alcohols are isolated and shown on further reaction to undergo cyclisation to give tetrahydroquinoline adducts. Therefore it is likely that in all these cases the pathway to the final tetrahydroquinoline adduct is via a multi-step process involving the amino-alcohol (or corresponding trifluoroacetate). Cyclisation of an iminium ion with the appropriate dienophile might be envisaged as a concerted aza-Diels Alder reaction. The evidence in this paper is to the contrary: the aza-Diels

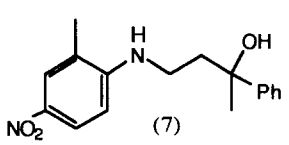
TABLE 1

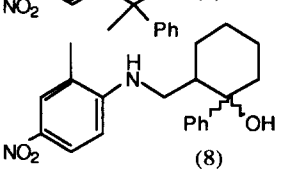
Reaction of 2-Methyl-4-nitroaniline with Formaldehyde and Electron Rich Alkenes

Amine	Alkene	Products	Yield (%)	Minor Products
	Styrene	 (1)	90	None
	α-Methylstyrene	 (2)	60	(5) (6) and (7)
		 (3)	80	(8)
		 (4)	73	None

 (5)

 (6)

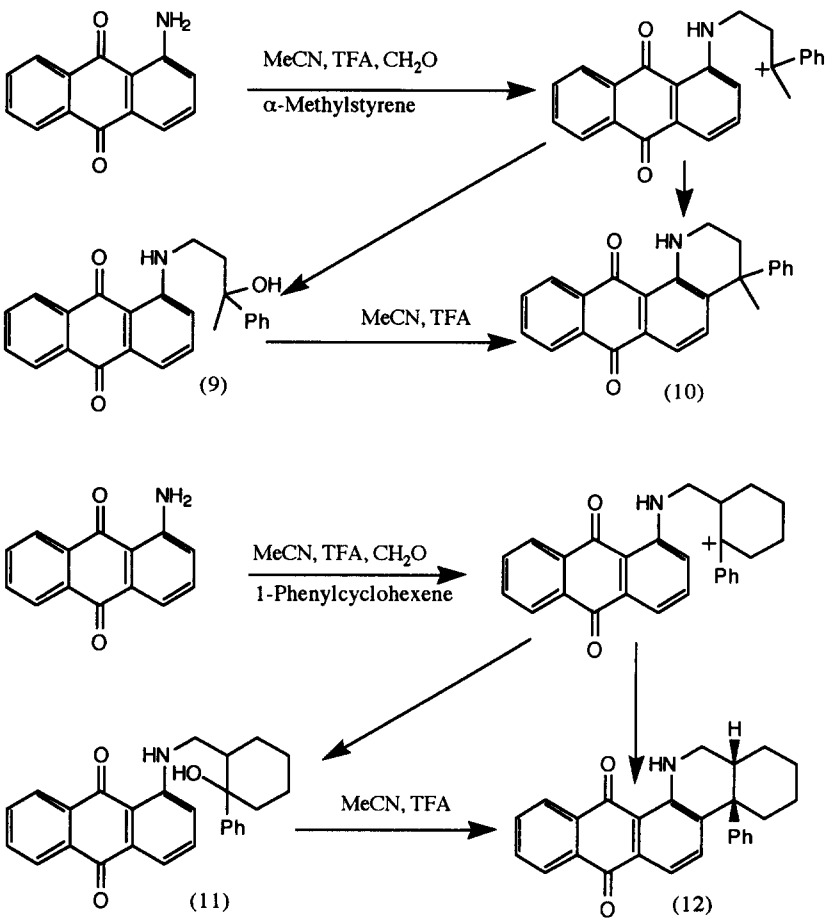
 (7)

 (8)

Alder adducts, the tetrahydroquinolines, are formed by multi-step sequences. These comments are reinforced by the behaviour of 1-phenylcyclohexene on reaction with formaldehyde and 2-methyl-4-nitroaniline. The major product is the tricyclic amine (3), assigned the *cis* stereochemistry by use of nOe experiments establishing the *cis* relation between the ring junction proton and the phenyl group. A minor product is the mixture of epimeric amino-alcohols (8), recognised by a doubling of signals in the ^{13}C NMR spectrum. The mixture of amino-

alcohols (8) could be separated from the tricyclic adduct (3) and on being heated in acetonitrile containing trifluoroacetic acid they were completely transformed to the tricyclic amine (3).

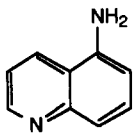
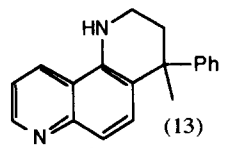
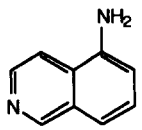
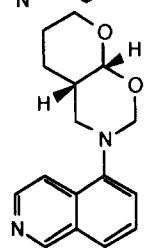
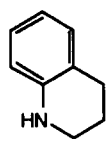
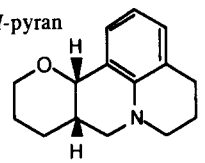
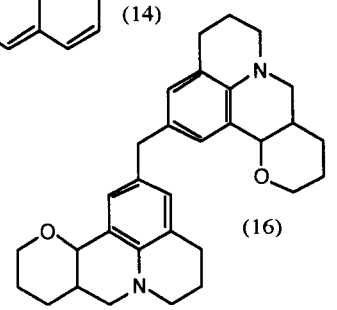
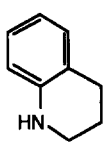
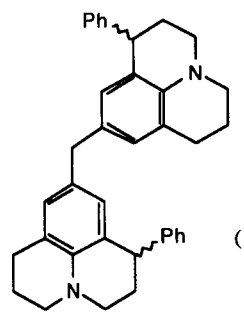
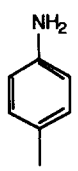
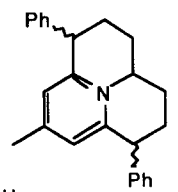
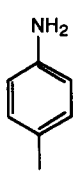
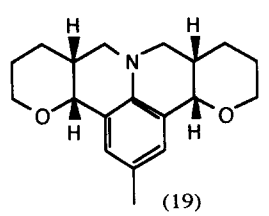
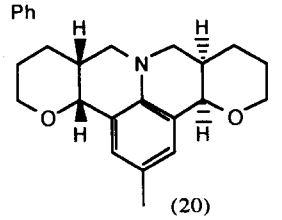
SCHEME1



Similar but more detailed studies have been made concerning the reaction of 1-aminoanthraquinone with α-methylstyrene and with 1-phenylcyclohexene (see Scheme 1). Reaction of α-methylstyrene afforded at room temperature two products, the intermediate amino-alcohol (9) (39% yield) and the tetracyclic amine (10) (56% yield). At room temperature the amino-alcohol (9) is slowly converted to the tetracycle (10). However under reflux in acetonitrile containing trifluoroacetic acid the amino-alcohol (9) is quantitatively cyclized to afford the amine (10). Similarly under the same reaction conditions at room temperature 1-phenylcyclohexene gave two products, the intermediate amino-alcohol (11) (15% yield) and the pentacyclic amine (12) (83%). Again the intermediate amino-alcohol (11) under reflux quantitatively affords the amine (12). These results confirm the existence of a multi-step mechanism for formation of the tetrahydroquinolines and suggest that all the tetrahydroquinolines described in this paper arise by a non-concerted pathway. The *cis* ring fusion in pentacyclic

TABLE 2

Reaction of Amines with Formaldehyde and Electron Rich Alkenes

Amine	Alkene	Products
	α-Methylstyrene	 (13)
	3,4-Dihydro-2*H*-pyran	 (14)
	3,4-Dihydro-2*H*-pyran	 (15)
		 (16)
	Styrene	 (17)
	Styrene	 (18)
	Dihydropyran	 (19)
		 (20)

(12) was established by nOe experiments in which irradiation of the ring junction proton caused an enhancement of the signal associated with the *ortho* protons of the phenyl group. Elsewhere[14] we describe related cyclocondensations of aminoanthraquinones with formaldehyde and various electron rich alkenes. Although in these examples intermediate amino-alcohols were not isolated, the results reported here and elsewhere[7,8,14] show that our methodology is a very effective high yielding route to diverse polycyclic anthraquinones. The efficiency of these cyclisations and those described above with 2-methyl-4-nitroaniline can, in part, be attributed to the activation of the intermediate iminium cation by the electron withdrawing nitro and carbonyl groups.

Further cyclocondensations, which are not so efficient, are collected in Table 2. In contrast to successful cyclocondensations involving cyclopentadiene with formaldehyde and aminoquinolines, which we have reported elsewhere[7,8], the reactions of styrenes with aminoquinolines are less efficient. Attempted reaction of 5-aminoisoquinoline with styrene failed to give any products which could be isolated. The outcome of the reaction between 5-aminoquinoline and α-methylstyrene is shown in Table 2. The anticipated adduct (13) could only be isolated in 6% yield, utilising the conditions which are more successful with activated systems. Similarly 5-aminoisoquinoline with 3,4-dihydro-2*H*-pyran gave as the only isolated product the pyrano[3,2-*e*][1,3]oxazine (14) in 50% yield. Evidently the cyclisation onto the heterocyclic system is not so favoured. In the above examples the difficulty is the lack of reactivity of the heterocyclic system to electrophiles. A further difficulty is experienced in reaction of tetrahydroquinoline with dihydropyran and with styrene. In the case of tetrahydroquinoline the problem stems from the ease with which the aromatic system reacts with electrophiles. It is found that reaction with dihydropyran gives the tetracycle (15) in 45% yield, but the product of further reaction (16) is isolated in 18% yield. Similarly reaction of tetrahydroquinoline with styrene gives the product (17) of further reaction in 49% yield. No doubt the isolation of tricyclic (18) from *p*-toluidine and styrene in only 23% yield can be attributed to similar complications. However even *p*-toluidine can afford products in good yield. The two crystalline diasteroisomers (19) and (20) were isolated separately in good overall yield (>80%). Their relative structural assignments are tentative. The isolation of products such as (16) and (17) is not unexpected in view of the ease with which formaldehyde reacts with nucleophilic aromatic compounds and have been encountered[7,8] elsewhere.

The results discussed in this paper extend the earlier studies of Grieco and Bahsas[3] in two important respects. Their one-pot procedure for synthesis of tetrahydroquinolines was confined to examples with cyclopentadiene. Here we show that results with other electron rich alkenes such as styrene, α–methylstyrene, 1-phenylcyclohexene and 3,4-dihydro-2*H*-pyran generalise the effectiveness of this approach to tetrahydroquinolines. In this and a further paper[14] describing results with other electron rich alkenes, cyclisations with cyclic alkenes afford *cis* fused adducts. The second important aspect of this paper is the clear demonstration that although these one-pot procedures might formally be considered to be examples of hetero-Diels Alder reactions, in reality they proceed by multi-step processes. Isolation of alcohols such as (11) and their cyclisation under the reaction conditions, *via* likely carbocation intermediates, provokes a more general question. It is implied[2-4] that a concerted cyclisation operates in the catalysed addition of electron rich alkenes to preformed imines. The results here suggest that multi-step cyclisations also occur in cyclisations based on preformed imines.

Experimental

Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 360MHz on a Bruker WH-360 spectrometer, at 270MHz on a Jeol JNM-GX-270 spectrometer or at 60MHz on a Hitachi-Perkin-Elmer R24-B spectrometer. ^{13}C NMR spectra were recorded at 68MHz on a Jeol JNM-GX-270 spectrometer or at 90MHz on a Bruker WH-360 spectrometer. In describing the ^{1}H and ^{13}C n.m.r. spectra, the numbering of the carbon atoms of the assigned signals is based on the numbering system of the starting aromatic amine. Infra-red spectra were recorded on a Perkin Elmer 298 spectrometer as chloroform solutions. Mass spectra (E. I.) were obtained using a VG Analytical 70-250-SE spectrometer. Analytical thin layer chromatography (tlc) was carried out using precoated silica gel plates (SIL G 25UV$_{254}$, 0.25mm, Macherey-Nagel) or precoated basic aluminium oxide plates (ALOX-25UV$_{254}$, 0.25mm, Macherey-Nagel). Flash chromatography was carried out using silica gel (C60 Sorbsil, May and Baker) or deactivated (3% by weight of water) basic aluminium oxide (pH 9.3-9.7, type 5016A, Fluka). Ether refers to diethyl ether and petrol refers to petroleum ether (b.p. 40-60^{o}C). All solvents were dried and freshly distilled before use. All compounds gave either satisfactory microanalytical data or were found to be homogeneous by tlc.

General Method: Cyclocondensation of 2-methyl-4-nitroaniline with formaldehyde and styrene

2-Methyl-4-nitroaniline (0.76g, 5mmol) was added to acetonitrile (14.3ml) containing one equivalent of trifluoroacetic acid (0.57g, 5mmol) to give a 0.35M amine concentration. To this yellow suspension was added with stirring a heterogeneous mixture of styrene (1.56 g, 15mmol) and 37% formalin solution (1.22ml, 15mmol) to give a yellow precipitate. The precipitate had failed to redissolve after 30min. of stirring at room temperature under nitrogen, so the mixture was heated at reflux under nitrogen for a further 30min, during which time the precipitate redissolved. After cooling the mixture was worked up to give an orange solid (2.13g) which was purified by preadsorption onto a minimum amount of deactivated basic alumina and loaded onto a deactivated alumina column. Flash chromatography afforded 1,2,3,4-tetrahydro-8-methyl-6-nitro-4-phenylquinoline (1) as a yellow solid(1.20g, 90%, eluant dichloromethane. Rf=0.70). (Rf of 2-methyl-4-nitroaniline=0.53. Rf values for basic alumina, 9/1 dichloromethane/petrol). Recrystallisation from methanol gave a yellow crystalline solid (m.p. 149 -151^{o}C) δH (270MHz) 7.87 (1H,d,J=2.3Hz,ArC$_5$-H); 7.63 (1H,d,J=2.3Hz,ArC$_3$-H); 7.19-7.40 (3H,m,Ar-H); 7.06 (2H,d,J=7.0Hz,Ar-H); 4.73 (1H,br.s,NH); 4.17 (1H,m,CH); 3.45 (1H,m,CH$_2$-N); 3.34 (1H,m, CH$_2$-N); 2.01-2.23 (5H,m,CH$_2$,ArC$_2$-CH$_3$). δC (68MHz) 148.92 (ArC$_1$-N); 144.73 (Cquat.); 136.75 (ArC$_4$-NO$_2$); 128.73 (ArC-H); 128.42 (ArC-H); 126.85 (ArC-H); 125.19 (ArC$_3$-H); 124.90 (ArC$_5$-H); 121.37 (ArC$_6$-C); 120.02 (ArC$_2$-CH$_3$); 42.69 (CH); 39.04 (CH$_2$-N); 29.33 (CH$_2$); 17.30 (ArC$_2$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3472, 3017, 2967, 2942, 2872, 1600, 1499, 1315, 1286 cm^{-1}. m/z [Found:- 268.1206 (M$^+$ 100%); 221(9); 207(10); 189(24); 144(7); 91((PhCH$_2$)$^+$ 11). $C_{16}H_{16}N_2O_2$ requires 268.1212] [Found:- C 71.4, H 5.9, N 10.4. $C_{16}H_{16}N_2O_2$ requires C 71.6, H 6.0, N 10.4%].

Reaction of 2-methyl-4-nitroaniline with formaldehyde and α-methylstyrene

2-Methyl-4-nitroaniline (1.52g, 10mmol) was added to acetonitrile (28.6ml) containing one equivalent of trifluoroacetic acid (1.14g, 10mmol) to give a 0.35M amine concentration. To this yellow suspension was added

with stirring a heterogeneous mixture of α-methylstyrene (3.55g, 30mmol) and 37% formalin solution (2.43ml, 30mmol) to give a yellow precipitate which redissolved after stirring at room temperature under nitrogen for 15min. The mixture was stirred at room temperature under nitrogen for a further 45min. and then worked up to give a yellow oil (5.43g) which was purified by chromatography on alumina to give 3,4,5,6-tetrahydro-6-methyl-3-(2-methyl-4-nitrophenyl)-6-phenyl-2*H*-[1,3]oxazine (5) as a yellow solid (0.76g, 24%, eluant 1/1 dichloromethane/petrol. Rf= 0.77); 1,2,3,4-tetrahydro-4,8-dimethyl-6-nitro-4-phenylquinoline (2) as a yellow solid(1.69g, 60%, eluant 4/1 dichloromethane/petrol. Rf=0.67); a diastereoisomeric mixture of the over-addition product 1,2,3,4-tetrahydro-1-(3-hydroxy-3-phenylbutyl)-4,8-dimethyl-6-nitro-4-phenylquinoline (6) as a yellow oil (0.20g, 5%, eluant 1/9 ethyl acetate/dichloromethane. Rf=0.33) and the alcohol *N*-(3-hydroxy-3-phenyl-butyl)-2-methyl-4-nitroaniline (7) as a yellow oil (0.30g, 10%, eluant 1/1 ethyl acetate/dichloromethane. Rf= 0.21). (Rf of 2-methyl-4-nitroaniline=0.50. Rf values for basic alumina, 9/1 dichloromethane/petrol). Recrystallisation of (5) from methanol gave yellow crystals (m.p. 110.5 - 113 °C). δH (270MHz) 8.04 (2H,m,ArC$_3$-H,ArC$_5$-H); 7.66 (1H,d,J=8.5Hz,ArC$_6$-H); 7.26-7.48 (5H,m,Ar-H); 4.82 (1H,br.d,J=11.4Hz, N-CH$_2$-O); 4.72 (1H,d,J=11.4Hz,N-CH$_2$-O); 3.29-3.48 (2H,m,CH$_2$-N); 2.29 (3H,s,ArC$_2$-CH$_3$); 2.20 (1H,dt,J=14.1,3.3Hz,CH$_2$); 1.97 (1H,ddd,J=14.1,10.4,5.0Hz,CH$_2$); 1.47 (3H,s,CH$_3$). δC (68MHz) 155.46 (ArC$_1$-N); 144.14 (Cquat.); 142.91 (ArC$_4$-NO$_2$); 132.37 (ArC$_2$-CH$_3$); 128.98 (ArC-H); 127.28 (ArC$_3$-H); 126.77 (ArC-H); 125.97 (ArC-H); 122.57 (ArC$_6$-H); 121.86 (ArC$_5$-H); 77.46 (N-CH$_2$-O); 76.55 (Cquat.-O); 46.91 (CH$_2$-N); 32.46 (CH$_3$); 32.12 (CH$_2$); 18.94 (ArC$_2$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 2990, 2940, 2890, 1608, 1587, 1494, 1342, 1273cm^{-1}. m/z [Found:- 312.1457 (M$^+$ 52%); 297(10); 194(22); 165((M-C$_{10}$H$_{11}$O)$^+$ 100); 132 (48); 118(63); 91((PhCH$_2$)$^+$ 16). $C_{18}H_{20}N_2O_3$ requires 312.1474]. [Found:- C 69.2, H 6.5, N 9.0. $C_{18}H_{20}N_2O_3$ requires C 69.2, H 6.45,N 9.0%].

Recrystallisation of (2) from methanol gave an orange crystalline solid (m.p. 157 - 159 °C). δH (270MHz) 7.92 (2H,br.s,ArC$_3$-H,ArC$_5$-H); 7.15-7.35 (3H,m,Ar-H); 7.06 (2H,d,J=7.9Hz,Ar-H); 4.67 (1H,br.s,NH); 3.41 (1H,m,CH$_2$-N); 3.09 (1H,brt,J=10.2Hz,CH$_2$-N); 2.14-2.28 (4H,m,CH$_2$,ArC$_2$-CH$_3$); 1.99 (1H,m,CH$_2$); 1.77 (3H,s,CH$_3$). δC (68MHz) 148.50 (ArC$_1$-N); 148.27 (Cquat.); 136.78 (ArC$_4$-NO$_2$); 128.53 (ArC-H); 127.02 (ArC-H); 126.47 (ArC-H); 126.07 (ArC$_6$-C); 124.90 (ArC$_3$-H); 123.62 (ArC$_5$-H); 119.98 (ArC$_2$-CH$_3$); 41.00 (Cquat.); 38.73 (CH$_2$-N); 36.78 (CH$_2$); 29.25 (CH$_3$); 17.58 (ArC$_2$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3475, 3020, 2985, 2945, 2875, 1602, 1525, 1498, 1315, 1293cm^{-1}. m/z [Found:- 282.1362 (M$^+$ 100%); 267((M-CH$_3$)$^+$ 75); 221(24); 203(18); 189(20); 91 (PhCH$_2$)$^+$ 33). $C_{17}H_{18}N_2O_2$ requires 282.1368]. [Found:- C 72.6, H 6.55, N 9.8. $C_{17}H_{18}N_2O_2$ requires C 72.3, H 6.4, N 9.9%].

An oily mixture of diastereoisomers of (6) were evidenced by the 'doubling up' of most signals in the ^{13}C spectrum:- δH (270MHz) 7.84 (2H,br.s,ArC$_3$-H,ArC$_5$-H); 7.15-7.40 (8H,m,Ar-H); 7.02 (2H,br.d,J= 7.3Hz, Ar-H); 2.96-3.22 (2H,m,CH$_2$-N); 2.68-2.90 (2H,m,CH$_2$-N); 2.10-2.35 (3H,m, CH$_2$,OH); 2.04 (3H,s,ArC$_2$-CH$_3$); 1.78-1.97 (2H,m,CH$_2$); 1.69 (3H,s,CH$_3$); 1.52 & 1.54 (3H,s,CH$_3$). δC (68MHz) 153.80 (Cquat.); 148.41 (ArC$_1$-N); 139.72 (ArC$_4$-NO$_2$); 135.64 (Cquat.); 128.86 & 128.92 (ArC$_6$-C); 128.49 (ArC-H); 127.16 (ArC-H); 127.11 (ArC-H); 126.46 (ArC-H); 126.23 (ArC$_3$-H); 124.80 & 124.84 (ArC$_2$-CH$_3$); 124.66 (ArC-H); 121.99 (ArC$_5$-H); 73.82 & 73.89 (Cquat.-O); 50.52 & 50.56 (CH$_2$-N); 46.13 (CH$_2$-N); 42.04 & 42.07

(Cquat.); 41.79 & 41.97($\underline{C}H_2$); 36.63 & 36.67 ($\underline{C}H_2$); 31.04 & 31.24 ($\underline{C}H_3$); 29.97 & 30.05 ($\underline{C}H_3$); 21.09 & 21.15 (ArC_2-$\underline{C}H_3$). $\nu_{max.}$($CHCl_3$):-3603 , 3440, 2978, 2860, 1591, 1495, 1315cm^{-1}. m/z [Found:- 430.2233 (M^+ 50%); 400(12); 295((M-$C_9H_{11}O)^+$ 100); 282(11); 265(11); 165(25); 91(($PhCH_2)^+$ 45). $C_{27}H_{30}N_2O_3$ requires 430.2256].

The oily alcohol (7) was characterized by δH (270MHz) 7.96 (1H,dd,J=9.0,2.3Hz,ArC_5-$\underline{H}$); 7.88 (1H,d,J=2.3Hz,ArC_3-$\underline{H}$); 7.23-7.50 (5H,m,Ar-$\underline{H}$); 6.32 (1H,d,J=9.0Hz,ArC_6-$\underline{H}$); 5.21 (1H,br.s,N$\underline{H}$); 3.26 (1H,m,$C\underline{H}_2$-N); 3.11 (1H,m,$C\underline{H}_2$-N); 2.23 (1H,br.s,O$\underline{H}$); 2.17 (2H,t,J=6.4Hz,$C\underline{H}_2$); 2.04 (3H,s,ArC_2-$C\underline{H}_3$); 1.68 (3H,s,$C\underline{H}_3$). δC (68MHz) 152.00 ($\underline{C}$quat.); 146.74 ($Ar\underline{C}_1$-N); 136.95 ($Ar\underline{C}_4$-NO_2); 128.67 ($Ar\underline{C}$-H); 127.23 ($Ar\underline{C}$-H); 126.00 ($Ar\underline{C}_3$-H); 124.93 ($Ar\underline{C}_5$-H); 124.64 ($Ar\underline{C}$-H); 121.19 ($Ar\underline{C}_2$-CH_3); 107.25 ($Ar\underline{C}_6$-H); 75.39 ($\underline{C}$quat.-O); 41.88 ($\underline{C}H_2$); 39.98 ($\underline{C}H_2$-N); 31.30 ($\underline{C}H_3$); 17.26 (ArC_2-$\underline{C}H_3$). $\nu_{max.}$($CHCl_3$):- 3610, 3415, 3015, 2983, 2935, 2875, 1610, 1593, 1530, 1494, 1325, 1294cm^{-1}. m/z [Found:- 300.1482 (M^+ 31%); 282((M-$H_2O)^+$ 5); 270(6); 165((M-$C_9H_{11}O)^+$ 100); 134(9); 118(34); 77(Ph^+ 7). $C_{17}H_{20}N_2O_3$ requires 300.1474].

It was found that decreasing the number of equivalents of formaldehyde and α-methylstyrene in the reaction gave the cycloadduct (2) and the intermediate aminoalcohol (7) as the only products.

2-Methyl-4-nitroaniline (0.76g, 5mmol) was added to acetonitrile (14.3ml) containing one equivalent of trifluoroacetic acid (0.57g, 5mmol) to give a 0.35M amine concentration. To this yellow suspension was added with stirring a heterogeneous mixture of α-methylstyrene (0.71g, 6mmol) and 37% formalin solution (0.49ml, 6mmol) to give a yellow precipitate which redissolved after stirring at room temperature under nitrogen for 1.5h. The mixture was stirred at room temperature under nitrogen for a further 30min. and then worked up to give a yellow oil (1.87g) which was purified by chromatography on alumina to give the adduct (2) as a yellow solid (1.01g, 72%) and the alcohol (7) as a yellow oil (0.41g, 27%).

Reaction of 2-methyl-4-nitroaniline with formaldehyde and 1-phenylcyclohexene

2-Methyl-4-nitroaniline (0.76g, 5mmol) was added to acetonitrile (14.2ml) containing one equivalent of trifluoroacetic acid (0.57g, 5mmol) to give a 0.35M amine concentration. To this deep yellow suspension was added with stirring a heterogeneous mixture of 1-phenylcyclohexene (2.37g, 15mmol) and 37% formalin solution (1.22ml, 15mmol) to give a yellow precipitate. The precipitate had failed to redissolve after 30min. of stirring at room temperature under nitrogen, so the mixture was heated at reflux under nitrogen for a further 30min, during which time the precipitate redissolved. After cooling the mixture was worked up to give a yellow oil (3.47g) which was purified by chromatography on alumina to give the adduct (6aα,10aα)-5,6,6a,7,8,9,10,10a-octahydro-4-methyl-2-nitro-10a-phenylphenanthridine (3) as a yellow solid (1.29g, 80%, eluant 4/1 dichloromethane/petrol. Rf=0.83) and an epimeric mixture of the alcohols *N*-{(2-hydroxy-2-phenylcyclohexyl)methyl}-2-methyl-4-nitroaniline (8) as a yellow oil (0.26g, 15%, eluant 1/9 ethyl acetate/dichloromethane. Rf=0.49). (Rf of 2-methyl-4-nitroaniline=0.56. Rf values for basic alumina, 9/1 dichloromethane/petrol). Recrystallisation of (3) from methanol gave a yellow crystalline solid (m.p. 231.5 - 234°C). δH (270MHz) 8.10 (1H,d,J=1.9Hz,ArC_5-$\underline{H}$); 7.97 (1H,d,J=1.9Hz,ArC_3-$\underline{H}$); 7.11-7.28 (3H,m,Ar-

H); 6.95 (2H,d,J=7.3Hz,Ar-H); 4.58 (1H,br.s,NH); 3.08 (1H,dd,J=12.2,3.5Hz,CH_2-N); 2.99 (1H,ddd, J=12.2,4.0,1.9Hz,CH_2-N); 2.49 (1H,br.d,J=14.3Hz,CH_2-CPh); 2.26 (1H,br.d,J=12.0Hz,CH); 2.16 (3H,s, ArC_2-CH_3); 2.04 (1H,br.t,J=12.7Hz,CH_2-CPh); 1.77 (1H,m,CH_2); 1.24-1.70 (5H,m,C H_2). δC (68MHz) 149.25 (Cquat.); 148.73 (ArC_1-N); 136.87 (ArC_4-NO_2); 128.62 (ArC-H); 126.95 (ArC-H); 126.44 (ArC-H); 125.03 (ArC_3-H); 124.30 (ArC_5-H); 120.35 (ArC_6-C); 119.78 (ArC_2-CH_3); 45.96 (Cquat.); 44.23 (CH_2-N); 38.44 (CH); 37.55 (CH_2-CPh); 27.76 (CH_2); 26.40 (CH_2); 22.49 (CH_2); 17.61 (ArC_2-CH_3). $\nu_{max.}$ ($CHCl_3$):- 3475, 3015, 2940, 2867, 1599, 1525, 1496, 1306, 1285cm^{-1}. m/z [Found:- 322.1668 (M^+ 100%); 265(51); 245(14); 219(12); 165($(M-C_{12}H_{13})^+$ 12); 91($(PhCH_2)^+$ 7). $C_{20}H_{22}N_2O_2$ requires 322.1681]. [Found:- C 74.3, H 6.8, N 8.7. $C_{20}H_{22}N_2O_2$ requires C 74.5, H 6.9, N 8.7%].

An epimeric mixture (~3:1 by ^1H n.m.r. integrations) of the alcohols (8) was characterised by δH (270MHz) 7.92 & 7.93 (1H,d,J=9.1Hz,ArC_5-H); 7.85 (1H,m,ArC_3-H); 7.54 (2H,d, J=7.0Hz,Ar-H); 7.28-7.40 (3H,m,Ar-H); 6.12 & 6.13 (1H,d,J=9.1Hz,ArC_6-H); 3.12 (1H, m,CH_2-N); 2.94 (1H,m,CH_2-N); 2.15 (2H,m,CH_2-CPh, NH); 1.85 & 1.93 (3H,s,ArC_2-CH_3); 1.40-1.90 (9H,m,CH,OH,CH_2-CPh,CH_2). δC (68MHz) The downfield (aromatic) region of the spectrum was very complex, but some signals were assignable. The presence of two diastereoisomers was confirmed by the 'doubling up' of most signals:- 151.31 & 152.01 (Cquat.); 146.93 & 147.39 (ArC_1-N); 121.00 (ArC_2-CH_3); 107.06 & 107.41 (ArC_6-H); 74.72 (Cquat.-O); 44.83 & 45.50 (CH); 45.35 (CH_2-N); 44.34 (CH_2-CPh); 26.20 & 26.84 (CH_2); 25.93 & 26.13 (CH_2); 21.25 & 21.88 (CH_2); 17.09 & 17.19 (ArC_2-CH_3). $\nu_{max.}$($CHCl_3$):- 3600, 3440, 3010, 2937, 2865, 1608, 1592, 1527, 1493, 1324, 1295cm^{-1}. m/z [Found:- 340.1783 (M^+ 34%); 323($(M-OH)^+$ 5); 165($(M-C_{12}H_{15}O)^+$ 100); 158 (59); 119(16); 105(14); 91($(PhCH_2)^+$ 9). $C_{20}H_{24}N_2O_3$ requires 340.1787].

The epimeric mixture of the intermediate aminoalcohols (8) was converted into the cycloadduct (3) by heating at reflux with trifluoroacetic acid in acetonitrile:-

The mixture of alcohols (8) (0.15g, 0.44mmol) was added to acetonitrile(5ml) to give a yellow suspension, trifluoroacetic acid (0.30g, 2.63mmol) was added and the mixture was heated at reflux under nitrogen. The reaction was monitored by t.l.c. analysis (basic alumina, 9/1 dichloromethane/petrol) which showed that after 2.5h only the cycloadduct (3) was present, the alcohols having gradually disappeared. After cooling the mixture was worked up to give the cycloadduct (3) as a yellow solid(0.15g, 100%). The t.l.c. characteristics, ^1H(270MHz) and ^{13}C(68MHz) n.m.r. spectra of this sample were identical to those for the cycloadduct obtained in the above cyclocondensation experiment. There was no trace of any *trans* fused cycloadduct.

Reaction of 2-methyl-4-nitroaniline with formaldehyde and 3,4-dihydro-2H-pyran

2-Methyl-4-nitroaniline (1.52g, 10mmol) was dissolved in acetonitrile (28.6ml) containing one equivalent of trifluoroacetic acid (1.14g, 10mmol) to give a 0.35M solution of the amine. To this yellow solution was added with stirring a heterogeneous mixture at 0°C of 3,4-dihydro-2*H*-pyran (1.01g, 12mmol) and 37% formalin solution (0.97ml, 12 mmol) to give a yellow precipitate. The precipitate had failed to redissolve after 1h of stirring at room temperature under nitrogen, so the mixture was heated at reflux under nitrogen for a further 30min, during which time the precipitate redissolved. After cooling the mixture was worked up to give a yellow

solid (3.06g) which was purified by chromatography on alumina to give (4aα,10bα)- 3,4,4a,5,6,10b-hexahydro-7-methyl-9-nitro-2*H*-pyrano[3,2-*c*]quinoline (4) as a yellow solid (1.82g, 73%, eluant 4/1 dichloromethane/petrol. Rf=0.41). (Rf of 2-methyl-4-nitroaniline=0.57. Rf values for basic alumina, 9/1 dichloromethane/petrol). Recrystallisation of (4) from methanol gave a yellow crystalline powder (m.p. 209.5 - 212.5 °C). δH (270MHz,DMSO-*d6*) 7.86 (1H,d,J=2.5Hz,ArC$_5$-H); 7.81 (1H,d,J=2.5Hz,ArC$_3$-H); 6.89 (1H,br.s,NH); 4.46 (1H,d,J=1.8Hz,CHO); 3.80 (1H,m,CH$_2$-O); 3.61 (1H,m,CH$_2$-O); 3.46 (1H,m,CH$_2$-N); 3.24 (1H,m,CH$_2$-N); 2.10 (3H,s,ArC$_2$-CH$_3$); 1.92 (1H,m,CH); 1.55-1.88 (3H,m,CH$_2$); 1.41 (1H,m,CH$_2$). δC (68MHz,DMSO-*d6*) 149.62 (ArC$_1$-N); 134.46 (ArC$_4$-NO$_2$); 125.23 (ArC$_3$-H); 125.08 (ArC$_5$-H); 120.71 (ArC$_2$-CH$_3$); 118.00 (ArC$_6$-C); 72.43 (CHO); 66.33 (CH$_2$-O); 40.47(CH$_2$-N); 30.23 (CH); 24.02 (CH$_2$); 21.89 (CH$_2$); 17.13 (ArC$_2$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3465, 3010, 2935, 2865, 1605, 1504, 1323, 1295 cm^{-1}. m/z [Found:- 248.1172 (M$^+$ 39%); 232(3); 218(8); 201(6); 189((M-C$_3$H$_7$O)$^+$ 100); 159 (8); 143(25). $C_{13}H_{16}N_2O_3$ requires 248.1161]. [Found:- C 62.6, H 6.5, N 11.0. $C_{13}H_{16}N_2O_3$ requires C 62.9, H 6.5, N 11.3%]

Reaction of 1-aminoanthraquinone, formaldehyde and α-methylstyrene

1-Aminoanthraquinone (1.12g, 5mmol) was added to acetonitrile(25ml) containing one equivalent of trifluoroacetic acid (0.57g, 5mmol) to give a 0.2M amine concentration. To this deep red/brown suspension was added with stirring a heterogeneous mixture of α-methylstyrene (1.78g, 15mmol) and 37% formalin solution (1.22ml, 15mmol). This deep red suspension was stirred at room temperature under nitrogen for 1.5h and then worked up to give a deep red oil (2.95g) which was purified by chromatography on alumina to give the adduct 1,2,3,4,7,12-hexahydro-4-methyl-7,12-dioxo-4-phenylnaphtho[2,3-*h*]quinoline (10) as a deep red oil (1.00g, 56%, eluant 2/3 dichloromethane/petrol. Rf= 0.62) and the alcohol 1-(3-hydroxy-3-phenylbutyl)amino-9,10-anthracenedione (9) as a deep red solid (0.73g, 39%, eluant 3/2 ethyl acetate/dichloromethane. Rf=0.14). (Rf of 1-aminoanthraquinone=0.33. Rf values for basic alumina, 1/1 ether/petrol). Recrystallisation of (10) from methanol gave a deep red crystalline powder (m.p. 129 - 132 °C). δH (270MHz) 10.27 (1H,br.s,NH); 8.29 (1H,dd,J=7.3,1.3Hz,ArC$_8$-H); 8.24 (1H,dd,J=7.3,1.3Hz,ArC$_5$-H); 7.73 (2H,m,ArC$_6$-H,ArC$_7$-H); 7.54 (1H, d,J=7.7Hz,ArC$_3$-H); 7.21-7.34 (4H,m,ArC$_4$-H,Ar-H); 7.13 (2H,d,J=7.0Hz,Ar-H); 3.50 (1H,ddd, J=13.0,8.8,4.3Hz,CH$_2$-N); 3.21 (1H,m,CH$_2$-N); 2.26 (1H,dt,J=13.3,4.8Hz,CH$_2$); 2.00 (1H,m,CH$_2$); 1.77 (3H,s,CH$_3$). Addition of three drops of D_2O with shaking caused the singlet at 10.27 (NH) to gradually diminish and a singlet at 4.80 (H_2O) slowly appeared (exchange was still incomplete after 77h). δC (68MHz) 184.84 (ArC$_9$=O); 183.86 (ArC$_{10}$=O); 149.34 (ArC$_1$-N); 147.98 (Cquat.); 137.08 (ArC$_2$-C); 135.46 (ArC$_{4a}$); 133.99 (ArC$_7$-H); 133.70 (ArC$_3$-H); 133.30 (ArC$_{8a}$); 133.17 (ArC$_{10a}$); 132.91 (ArC$_6$-H); 128.60 (ArC-H); 127.05 (ArC$_8$-H); 126.85 (ArC-H); 126.77 (ArC$_5$-H); 126.60 (ArC-H); 115.57 (ArC$_4$-H); 111.87 (ArC$_{9a}$); 41.58 (Cquat.); 37.76 (CH$_2$-N); 36.01 (CH$_2$); 28.88 (CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3275, 3020, 2970, 2875, 1663, 1624, 1597,1577, 1520cm^{-1}. m/z [Found:- 353.1406 (M$^+$ 100%); 338((M-CH$_3$)$^+$ 72); 274(23); 260(18); 169(5); 91 ((PhCH$_2$)$^+$ 16). $C_{24}H_{19}NO_2$ requires 353.1416].

Recrystallisation of (9) from methanol gave a deep red crystalline powder (m.p. 172.5 - 174.5 °C). δH

(270MHz) 9.71 (1H,br.s,NH); 8.22 (2H,m,ArC$_5$-H,ArC$_8$-H); 7.71 (2H,m,ArC$_6$-H, ArC$_7$-H); 7.24-7.55 (7H,m,ArC$_3$-H,ArC$_4$-H,Ar-H); 6.87 (1H,d,J=8.5Hz,ArC$_2$-H); 3.35 (1H,m,CH$_2$-N); 3.19 (1H,m,CH$_2$-N); 2.26 (2H,t,J=7.5Hz,CH$_2$); 2.12 (1H,br.s,OH); 1.69 (3H,s,CH$_3$). Addition of three drops of D_2O with shaking caused the singlets at 9.71 (NH) and 2.12 (OH) to disappear and a singlet at 4.85 (H_2O) appeared (although exchange was slow). δC (68MHz) 185.00 (ArC$_9$=O); 184.04 (ArC$_{10}$=O); 151.68 (Cquat.); 147.05 (ArC$_1$-N); 136.42 (ArC$_{4a}$); 135.37 (ArC$_3$-H); 135.15 (ArC$_{8a}$); 134.74 (ArC$_{10a}$); 134.09 (ArC$_7$-H); 133.04 (ArC$_6$-H); 128.60 (ArC-H); 127.12 (ArC$_8$-H); 126.85 (ArC$_5$-H,ArC-H); 124.79 (Ar C-H); 118.03 (ArC$_2$-H); 115.77 (ArC$_4$-H); 113.12 (ArC$_{9a}$); 74.39 (Cquat.-O); 43.02 (CH$_2$); 38.92 (CH$_2$-N); 31.27 (CH$_3$). $\nu_{max.}$($CHCl_3$):- 3600, 3300, 3015, 1670, 1632, 1598, 1575, 1507cm^{-1}. m/z [Found:- 371.1516 (M^+ 20%); 353((M-H_2O)$^+$ 19); 251(43); 236((M-$C_9H_{11}O$)$^+$ 100); 223(13); 165(8); 152(10). $C_{24}H_{21}NO_3$ requires 371.1521. [Found:- C 78.0, H 5.6, N 3.6. $C_{24}H_{21}NO_3$ requires C 77.6, H 5.7, N 3.8%]

The intermediate aminoalcohol (9) was converted into the cycloadduct (10) by heating at reflux with trifluoroacetic acid in acetonitrile:- The alcohol (9) (0.09g, 0.24mmol) was added to acetonitrile (8ml) to give a deep red suspension, trifluoroacetic acid (0.08g, 0.70mmol) was added and the mixture was stirred at room temperature under nitrogen. The reaction was monitored by t.l.c. analysis (basic alumina, 1/1 ether/petrol) which showed that the alcohol (9) was still the only compound present after 1h. More trifluoroacetic acid (0.08g, 0.70mmol) was added and the mixture was then heated at reflux under nitrogen. After 20min. t.l.c. analysis showed that some cycloadduct (10) was present and after 1h only the cycloadduct (10) was present, the alcohol (9) having disappeared. After cooling the mixture was worked up to give the cycloadduct (10) as a deep red oil (0.09g, 100%). The t.l.c. characteristics, ^{1}H(270MHz) and ^{13}C(68MHz) n.m.r. spectra of this sample were identical to those for the cycloadduct obtained in the above cyclocondensation experiment.

Two further cyclocondensation experiments were carried out in order to assess the effect of temperature on the yields of the cycloadduct (10) and the intermediate amino-alcohol (9):-

1-Aminoanthraquinone (0.56g, 2.5mmol) was added to acetonitrile (13ml) containing one equivalent of trifluoroacetic acid (0.29g, 2.5mmol) to give a 0.2M amine concentration. To this deep red/brown suspension was added with stirring a heterogeneous mixture of α-methylstyrene (0.89g, 7.5mmol) and 37% formalin solution (0.61ml, 7.5mmol). This deep red suspension was heated at reflux under nitrogen for 1.5h and then after cooling the mixture was worked up to give a deep red oil (1.46g) which was purified by chromatography on alumina to give the adduct (10) as a deep red oil (0.73g, 82%) and the alcohol (9) as a deep red solid (0.16g, 17%).

1-Aminoanthraquinone (0.56g, 2.5mmol) was added to acetonitrile (13ml) containing one equivalent of trifluoroacetic acid (0.29g, 2.5mmol) to give a 0.2M amine concentration. To this deep red/brown suspension was added with stirring a heterogeneous mixture of α-methylstyrene (0.89g, 7.5mmol) and 37% formalin solution (0.61ml, 7.5mmol). This deep red suspension was stirred at 0°C under nitrogen for 3h and then worked up to give a deep red solid (1.33g) which was purified as above to give the adduct (10) as a deep red oil (0.33g, 37%); the alcohol (9) as a deep red solid (0.22g, 24%) and recovered 1-aminoanthraquinone as an orange solid (0.10g, 18%, eluant dichloromethane).

Reaction of 1-aminoanthraquinone with formaldehyde and 1-phenylcyclohexene

1-Aminoanthraquinone (0.56g, 2.5mmol) was added to acetonitrile (13ml) containing one equivalent of trifluoroacetic acid (0.29g, 2.5mmol) to give a 0.2M amine concentration. To this deep red/brown suspension was added with stirring a heterogeneous mixture of 1-phenylcyclohexene (1.19g, 7.5mmol) and 37% formalin solution (0.61ml, 7.5mmol). This deep red suspension was heated at reflux under nitrogen for 1h and then after cooling the mixture was worked up to give a deep red oil (2.00g) which was purified by chromatography on alumina to give (4aα,14aα)- 1,2,3,4,4a,7,12,13,14,14a-decahydro-7,12-dioxo-4a-phenylnaphtho[2,3-*c*]phenanthridine (12) as a deep red oil (0.82g, 83%, eluant 1/1 dichloromethane/petrol. Rf=0.65) and an epimeric mixture of 1-{(2-hydroxy-2-phenylcyclohexyl)methyl}amino-9,10-anthracenedione (11) as a deep red oil(0.15g, 15%, eluant 1/1 ethyl acetate/dichloromethane. Rf=0.24). (Rf of 1-aminoanthraquinone= 0.27. Rf values for basic alumina, 1/1 ether/petrol). Recrystallisation of (12) from methanol gave a deep red crystalline powder (m.p. 131 - 134 °C). δH (360MHz) 10.22 (1H,d,J=4.0Hz,NH); 8.30 (2H,m,ArC$_5$-H,ArC$_8$-H); 7.75 (2H,m,ArC$_6$-H,ArC$_7$-H); 7.70 (1H,d,J=7.8Hz,ArC$_4$-H); 7.59 (1H,d,J=7.8Hz,ArC$_3$-H); 7.16-7.31 (3H,m, Ar-H); 7.05 (2H,d,J=7.3Hz,Ar-H); 3.16 (1H,dd,J=13.0,4.0Hz,CH$_2$-N); 3.06 (1H,ddd,J=13.0,4.7,1.8Hz, CH$_2$-N); 2.49 (1H,br.d,J=15.0Hz,CH$_2$-CPh); 2.29 (1H,br.d,J=12.2Hz,CH); 2.06 (1H,m,CH$_2$-CPh); 1.80 (1H,m,CH$_2$); 1.35-1.70 (5H,m,CH$_2$). δC (90MHz) 184.67 (ArC$_9$=O); 183.85(ArC$_{10}$=O); 149.43 (ArC$_1$-N); 148.61(Cquat.); 135.40(ArC$_{4a}$); 134.41(ArC$_3$-H); 133.87 (ArC$_7$-H); 133.23 (ArC$_{8a}$); 133.19 (ArC$_{10a}$); 132.75 (ArC$_6$-H); 131.62 (ArC$_2$-C); 128.63 (ArC-H); 126.83 (ArC-H); 126.72 (ArC$_8$-H); 126.64 (ArC-H); 126.49 (ArC$_5$-H); 115.34 (ArC$_4$-H); 111.53 (ArC$_{9a}$); 46.50 (Cquat.); 43.21 (CH$_2$-N); 38.06 (CH); 37.58 (CH$_2$-CPh); 27.82 (CH$_2$); 26.34 (CH$_2$); 22.46(CH$_2$). The structure and assignments were confirmed by ^{1}H decoupled, ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY and nOe. spectra. $\nu_{max.}$(CHCl$_3$):- 3275, 3070, 3045, 3020, 2950, 2870, 1665, 1622, 1595, 1575, 1519 cm^{-1}. m/z [Found:- 393.1752 (M$^+$ 100%); 336(47); 316(12); 286(11); 260(11); 236((M-C$_{12}$H$_{13}$)$^+$ 17). $C_{27}H_{23}NO_2$ requires 393.1729] [Found:- C 82.6, H 5.8, N 3.4. $C_{27}H_{23}NO_2$ requires C 82.4, H 5.9, N 3.6%].

An epimeric mixture (~2:1 by ^{1}H n.m.r. integrations) of the alcohols (11) was characterized by δH (270MHz) 9.72 (1H,m,NH); 8.22 (2H,m,ArC$_5$-H,ArC$_8$-H); 7.70 (2H,m, ArC$_6$-H,ArC$_7$-H); 7.51 (2H,m,ArC$_3$-H, ArC$_4$-H); 7.20-7.45 (5H,m,Ar-H); 6.51 & 6.56 (1H,d,J= 8.7Hz,ArC$_2$-H); 3.09 (2H,m,CH$_2$-N); 1.35-2.35 (10H,m,CH,OH,CH$_2$-CPh,CH$_2$). δC (68MHz) The downfield (aromatic) region of the spectrum was very complex, but some signals were assignable.The presence of two diastereoisomers was confirmed by the 'doubling up' of most signals:- 184.90 (ArC$_9$=O); 147.51 (ArC$_1$-N); 118.05 & 118.18 (ArC$_2$-H); 115.56 & 115.64 (ArC$_4$-H); 74.25 & 75.69 (Cquat.-O); 45.02 & 45.39 (CH); 44.01 (CH$_2$-N); 41.71 & 41.85 (CH$_2$-CPh); 25.81 & 26.63 (CH$_2$); 22.00 & 23.84 (CH$_2$); 21.23 & 21.69 (CH$_2$). $\nu_{max.}$(CHCl$_3$):- 3605, 3300, 3010, 2940, 2870, 1670, 1630, 1598, 1580, 1515 cm^{-1}. m/z [Found:- 411.1806 (M$^+$ 57%); 393((M-H$_2$O)$^+$ 4); 236((M-C$_{12}$H$_{15}$O)$^+$ 100); 223 (15); 208(6); 165(6); 105(8). $C_{27}H_{25}NO_3$ requires 411.1834].

The epimeric mixture of the intermediate aminoalcohols (11) was converted into the cycloadduct (12) by heating at reflux with trifluoroacetic acid in acetonitrile:- The mixture of alcohols (11) (0.16g, 0.39mmol) was

added to acetonitrile (5ml) to give a deep red suspension, trifluoroacetic acid (0.27g, 2.37mmol) was added and the mixture was heated at reflux under nitrogen. The reaction was monitored by t.l.c. analysis (basic alumina, 1/1 ether/petrol) which showed that after 3h only the cycloadduct (12) was present, the alcohols (11) having gradually disappeared. After cooling the mixture was worked up to give the cycloadduct (12) as a deep red oil(0.12g, 80%). The t.l.c. characteristics, ^{1}H(270MHz) and ^{13}C(68MHz) n.m.r. spectra of this sample were identical to those for the cycloadduct obtained in the above cyclocondensation experiment. There was no trace of any *trans* fused cycloadduct. A further cyclocondensation experiment was carried out in order to assess the effect of temperature on the yields of the cycloadduct (12) and the epimeric intermediate aminoalcohols (11):- 1-Aminoanthraquinone (1.12g, 5mmol) was added to acetonitrile (25ml) containing one equivalent of trifluoroacetic acid (0.57g, 5mmol) to give a 0.2M amine concentration. To this deep red/brown suspension was added with stirring a heterogeneous mixture of 1-phenylcyclohexene (2.38g, 15mmol) and 37% formalin solution (1.22ml, 15mmol). This deep red suspension was stirred at room temperature under nitrogen for 6h and then worked up to give a deep red oil (3.43g) which was purifiedby chromatography on alumina to give the adduct (12) as a deep red oil (0.79g, 41%); an epimeric mixture of the alcohols (11) as a deep red oil (0.53g, 26%) and recovered 1-aminoanthraquinone as an orange solid (0.28g, 25%, eluant dichloromethane).

Reaction of 5-aminoquinoline with formaldehyde and α-methylstyrene

5-Aminoquinoline (0.61g, 4.24mmol) was dissolved in acetonitrile (12.1ml) containing two equivalents of trifluoroacetic acid (0.97g, 8.51mmol) to give a 0.35M solution of the amine. To this orange solution was added with stirring a heterogeneous mixture of α-methylstyrene (0.60g, 5.08mmol) and 37% formalin solution (0.41ml, 5.06 mmol) to give an orange precipitate which was stirred at room temperature under nitrogen for 2.5h. Work up afforded a deep red oil (1.05g) which was purified by chromatography on alumina to give 1,2,3,4-tetrahydro-4-methyl-4-phenyl[1,7]phenanthroline (13) as a yellow oil (0.07g, 6%, eluant ether. Rf=0.56) and recovered 5-aminoquinoline as a yellow/orange solid (0.18g, 30%, eluant 3/1 ether/ethyl acetate. Rf= 0.41). (Rf values for basic alumina, ether). Recrystallisation of (13) from methanol gave a yellow/brown solid (m.p. 167.5 - 171 °C). δH (270MHz) 8.82 (1H,br.d,J=2.9Hz,ArC$_2$-H); 8.11 (1H,br.d,J=8.5Hz,ArC$_4$-H); 7.41 (1H,d,J=8.9Hz,ArC$_8$-H); 7.10-7.48 (7H,m,ArC$_7$-H,ArC$_3$-H,Ar-H); 4.70 (1H,br.s,NH); 3.38 (1H, m,CH$_2$-N) ; 3.19 (1H,ddd,J=12.6,8.2,3.2Hz,CH$_2$-N); 2.23 (1H,ddd,J=12.4,5.7,3.2Hz,CH$_2$); 2.07 (1H, ddd,J=12.4,8.2,3.8Hz,CH$_2$); 1.81 (3H,s,CH$_3$). δC (68MHz) 150.27 (Cquat.); 149.64 (ArC$_2$-H); 148.14 (ArC$_{8a}$); 139.24 (ArC$_5$-N); 131.25 (ArC$_7$-H); 128.89 (ArC$_4$-H); 128.19 (ArC-H); 127.51 (ArC-H); 125.97 (ArC-H); 122.67 (ArC$_6$-C); 119.46 (ArC$_3$-H); 118.11 (ArC$_{4a}$); 117.92 (ArC$_8$-H); 40.97 (Cquat.); 39.12 (CH$_2$-N); 38.80 (CH$_2$); 29.48 (CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3453, 3073, 2973, 2868, 1581, 1516, 1487cm^{-1}. m/z [Found:- 274.1466 (M$^+$ 95%); 259((M-CH$_3$)$^+$ 100); 197(35); 181 (23); 157(20); 129(13); 91((PhCH$_2$)$^+$ 23). $C_{19}H_{18}N_2$ requires 274.1470]

Reaction of 5-aminoisoquinoline with formaldehyde and 3,4-dihydro-2*H*-pyran

5-Aminoisoquinoline(0.36g, 2.5mmol) was dissolved in acetonitrile (3.6ml) containing two equivalents of trifluoroacetic acid (0.58g, 5mmol) to give a 0.7M solution of the amine. This yellow solution was added with stirring to a heterogeneous mixture at 0°C of 3,4-dihydro-2*H*-pyran (0.42g, 5mmol) and 37% formalin solution (0.41ml, 5mmol). The mixture was stirred at room temperature under nitrogen for 30min. and then worked up to give a yellow oil (0.86g) which was purified by chromatography to give (4aα,8aα)- 3,4,4a,6,7,8a-hexahydro-3-(5-isoquinolyl)-2*H*,5*H*-pyrano[3,2-*e*][1,3]oxazine (14) as a yellow solid (0.34g, 50%, eluant 7/3 ether/ethyl acetate. Rf=0.50) and recovered 5-aminoisoquinoline as a yellow/orange solid (0.08g, 22%, eluant 1/4 ether/ethyl acetate. Rf=0.32). (Rf values for basic alumina, 3/1 ether/ethyl acetate).

Recrystallisation of (14) from ether gave a cream solid (m.p. 101 - 103.5 °C). δH (270MHz) 9.23 (1H,s,ArC$_1$-H); 8.53 (1H,d,J=6.0Hz,ArC$_3$-H); 7.87 (1H,d,J=6.0Hz,ArC$_4$-H); 7.73(1H,br.d,J=8.0Hz,ArC$_6$-H); 7.68 (1H,d,J=8.0Hz,ArC$_8$-H); 7.52 (1H,t,J= 8.0Hz,ArC$_7$-H); 5.29 (1H,d,J=10.4Hz,N-CH$_2$-O); 5.03 (1H,d,J= 2.5Hz,O-CH-O); 4.75 (1H,d,J=10.4Hz,N-CH$_2$-O); 4.11 (1H,m,CH$_2$-O); 3.81 (1H,m,CH$_2$-N); 3.65 (1H,m,CH$_2$-O); 3.36 (1H,m,CH$_2$-N); 2.04 (1H,m,CH); 1.40-1.78 (4H,m,CH$_2$). δC (68MHz) 153.18 (ArC$_1$-H); 145.91 (ArC$_5$-N); 142.93 (ArC$_3$-H); 131.48 (ArC$_{4a}$); 130.04 (ArC$_{8a}$); 127.44 (ArC$_7$-H); 123.09 (ArC$_8$-H); 121.52 (ArC$_6$-H); 116.75 (ArC$_4$-H); 97.85 (O-CH-O); 78.81 (N-CH$_2$-O)*; 65.39 (CH$_2$-O)*; 51.80 (CH$_2$-N)*; 32.46 (CH)*; 24.78 (CH$_2$); 22.44 (CH$_2$). (Note signals marked * were broad and of weak intensity). $\nu_{max.}$(CHCl$_3$):- 2960, 2875, 1623, 1588, 1490cm^{-1}. m/z [Found:- 270.1379 (M$^+$ 26%); 240((M-CH$_2$O)$^+$ 5); 167(2); 156((M-C$_6$H$_{10}$O$_2$)+ 100); 149(3); 129(11); 101(4). C$_{16}$H$_{18}$N$_2$O$_2$ requires 270.1368]. Two further experiments were carried out in order to assess the effect of varying the number of equivalents of formaldehyde and 3,4-dihydro-2*H*-pyran in the reaction:- 5-Aminoisoquinoline (0.22g, 1.53mmol) was dissolved in acetonitrile (2.2ml) containing two equivalents of trifluoroacetic acid(0.35g, 3.07mmol) to give a 0.7M solution of the amine. This yellow solution was added with stirring to a heterogeneous mixture at 0°C of 3,4-dihydro-2*H* -pyran(0.26g, 3.10mmol) and 37% formalin solution (0.50ml, 6.17mmol). The mixture was stirred at room temperature under nitrogen for 30min. and then worked up to give a yellow oil (0.63g) which was purified by chromatography on alumina to give the title pyrano[1,3]oxazine (14) as a yellow solid (0.24g, 58%) and recovered 5-aminoisoquinoline as a yellow/orange solid(0.04g, 18%).

5-Aminoisoquinoline(0.22g, 1.53mmol) was dissolved in acetonitrile (2.2ml) containing two equivalents of trifluoroacetic acid (0.35g, 3.07mmol) to give a 0.7M solution of the amine. This yellow solution was added with stirring to a heterogeneous mixture at 0 °C of 3,4-dihydro-2*H*-pyran(0.51g, 6.07mmol) and 37% formalin solution (0.99ml, 12.21mmol). The mixture was stirred at room temperature under nitrogen for 30min. and then worked up to give a yellow oil (0.82g) which was purified by chromatography on alumina to give the title pyrano[1,3]oxazine (14) as a yellow solid (0.16g, 39%) and recovered 5-aminoisoquinoline as a yellow/orange solid(0.03g, 14%).

Reaction of 1,2,3,4-tetrahydroquinoline with formaldehyde and 3,4-dihydro-2*H*-pyran

1,2,3,4-Tetrahydroquinoline (0.80g, 6mmol) was dissolved in acetonitrile (8.6ml) containing one equivalent of trifluoroacetic acid (0.69g, 6mmol) to give a 0.7M solution of the amine. This pale yellow solution was added with stirring to a heterogeneous mixture at 0°C of 3,4-dihydro-2*H* -pyran (1.01g, 12mmol) and 37% formalin solution(0.49ml, 6 mmol) to give a dark green solution after 5min. which was stirred at room temperature under nitrogen for 20min. Work up afforded a yellow/brown oil (1.72g) which was purified by chromatography on alumina to give (8aα,12aα)- 5,6, 8a,10,11,12a-hexahydro-4*H*,8*H*,9*H* -pyrano[3,2-*c*]pyrido[3,2,1-*ij*]quinoline (15) as a pale yellow oil (0.62g, 45%, eluant 1/4 ether/petrol. Rf=0.58) along with the para-coupled 'dimer' 2,2'-methylenebis(5,6,8a,10,11,12a-hexahydro-4*H*,8*H*,9*H* -pyrano[3,2-c]pyrido[3,2,1-*ij*]quinoline (16) as a pale yellow oil (0.25g, 18%, eluant 1/1 ether/petrol. Rf=0.26). (Rf of 1,2,3,4-tetrahydroquinoline=0.58. Rf values for basic alumina, 1/1 ether/petrol). The adduct (15) was characterized by δH (360MHz) 7.05 (1H,br.d,J=7.4Hz,ArC$_7$-H); 6.86 (1H,br.d,J=7.4Hz,ArC$_5$-H); 6.55 (1H,t,J=7.4Hz,ArC$_6$-H); 4.42 (1H, d,J=2.9Hz,CHO); 3.99 (1H,m,CH$_2$-O); 3.69 (1H,m, CH$_2$-O); 3.49 (1H,m,CH$_2$-N); 3.17 (2H,m,C$_2$H$_2$-N); 2.88 (1H,ddd,J=11.0,4.0,1.2Hz,CH$_2$-N); 2.79 (2H,m,Ar-C$_4$H$_2$); 2.16 (1H,m,CH); 1.78-2.07 (5H,m, C$_3$H$_2$,CH$_2$); 1.47 (1H,m,CH$_2$). δC (90MHz) 142.94 (ArC$_{8a}$-N); 129.21 (ArC$_5$-H); 128.76 (ArC$_7$-H); 121.96 (ArC$_8$-C); 120.81 (ArC$_{4a}$); 116.19 (ArC$_6$-H); 74.44 (CHO); 67.63 (CH$_2$-O); 49.95 (CH$_2$-N); 49.90 (C$_2$H$_2$-N); 32.21 (CH); 27.67 (Ar-C$_4$H$_2$); 25.75 (CH$_2$); 22.72 (CH$_2$); 22.04 (C$_3$H$_2$).

The structure and assignments were confirmed by ^{1}H-^{1}H and ^{1}H-^{13}C COSY spectra. [Note in the ^{13}C(68MHz) spectrum in $CDCl_3$, the signals for CH$_2$-N and C$_2$H$_2$-N were synchronous at 49.96ppm. However, the spectrum in DMSO-*d*6 showed two signals at 48.90 and 48.99ppm]. $\nu_{max.}$($CHCl_3$):- 3010, 2945, 2855, 1604, 1495, 1450 cm^{-1}. m/z [Found:- 229.1455 (M^+ 57%); 200(4); 184(8); 170((M-C_3H_7O)$^+$ 100); 154(5); 146 (10); 130(5). $C_{15}H_{19}NO$ requires 229.1467].

The para-coupled 'dimer' (16) was characterized by- δH (270MHz) 6.86 (2H,s,ArC$_7$-H); 6.68 (2H,s,ArC$_5$-H); 4.34 (2H,m,CHO); 3.95 (2H,m, CH$_2$-O); 3.63 (4H,m,CH$_2$-O,Ar-CH$_2$-Ar); 3.41(2H,m,CH$_2$-N); 3.09 (4H,m,C$_2$H$_2$-N); 2.80(2H,dd,J=11.0,3.5Hz,CH$_2$-N); 2.60-2.75 (4H,m,Ar-C$_4$H$_2$); 0.85-2.12 (14H,m, C$_3$H$_2$,CH$_2$,CH). δC (68MHz) 141.09 (ArC$_{8a}$-N); 129.94 (ArC$_5$-H); 129.09 (ArC$_7$-H); 122.17 (ArC$_8$-C); 120.81 (ArC$_{4a}$); 74.54 (CHO); 67.75 (CH$_2$-O); 50.06 (CH$_2$-N,C$_2$H$_2$-N); 40.25 (Ar- CH$_2$-Ar); 32.46 (CH); 27.61 (Ar-C4H$_2$); 25.94 (CH$_2$); 22.7 (CH$_2$); 22.27 (C$_3$H$_2$). (Note the signal for ArC$_6$-CH$_2$Ar was obscured). $\nu_{max.}$($CHCl_3$):- 3007, 2940, 2853, 1618, 1502, 1460 cm^{-1}. m/z [Found:- 470.2909 (M^+ 4%); 331(7); 246(6); 229((M-$C_{16}H_{19}NO$)$^+$ 13); 170((M-$C_{19}H_{26}NO_2$)$^+$ 28); 146((M-$C_{21}H_{26}NO_2$)$^+$ 100); 132(18). $C_{31}H_{38}N_2O_2$ requires 470.2933]. A second isomer of the para-coupled 'dimer' was not isolated.

Reaction of 1,2,3,4-tetrahydroquinoline with formaldehyde and styrene

1,2,3,4-Tetrahydroquinoline (1.33g, 10mmol) was dissolved in acetonitrile (7.1ml) containing one equivalent of trifluoroacetic acid (1.14g, 10mmol) to give a 1.4M solution of the amine. This pale brown solution was added with stirring to a heterogeneous mixture of styrene(5.20g, 50mmol) and 37% formalin solution(4.05ml, 50mmol) and the mixture was stirred at room temperature under nitrogen for 1.5h. Work up afforded a deep red

oil (5.71g) which was purified by chromatography on silica gel to give a diastereoisomeric mixture of the para-coupled 'dimer' 9,9'-methylenebis-(2,3,6,7-tetrahydro-1-phenyl-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline) (17) (mixture of (1α,1'α)- and (1 α,1'β)-) as a red/brown oil [1.24g, 49%, eluant dichloromethane. Rf=0.49 (silica gel, dichloromethane)] δH (270MHz) 7.15-7.35 (6H,m,Ar-H); 7.08 (4H,d,J=6.7Hz,Ar-H); 6.57 (2H,s,ArC_7-H); 6.39 (2H,s,ArC_5-H); 4.08 (2H,t,J=6.4Hz,CH); 3.44 (2H,s,Ar-CH_2-Ar); 3.10-3.15 (8H,m,C_2H_2-N,CH_2-N); 2.76 (4H,t,J=6.5Hz,Ar-C_4H_2); 2.31 (2H,m,CH_2); 2.08 (6H,br.m,C_3H_2,CH_2). $\nu_{max.}$ ($CHCl_3$):- 3010 ,2950, 2840, 2800, 1615, 1495, 1465 cm^{-1}. m/z [Found:- 510 (M^+ 100%); 431(5); 406(5); 378(5); 262((M-$C_{18}H_{18}N)^+$ 20); 248 ((M-$C_{19}H_{20}N)^+$ 3); 203(26). $C_{37}H_{38}N_2$ requires 510].

Reaction of *p*-toluidine with formaldehyde and styrene

p-Toluidine (2.14g, 20mmol) was dissolved in acetonitrile (14.3ml) containing one equivalent of trifluoroacetic acid (2.28g, 20mmol) to give a 1.4M solution of the amine. This brown solution was added with stirring to a heterogeneous mixture of styrene (10.40g, 100mmol) and 37% formalin solution (8.11ml, 100mmol) to give a deep red solution which was stirred at room temperature under nitrogen for 3h. Work up afforded a pale brown oily solid (9.06g) which was purified by chromatography on silica gel to give a diastereoisomeric mixture of 2,3,6,7-tetrahydro-9-methyl-1,7-diphenyl-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline (18) (mixture of (1α,7β)- and (1 α,7α)-) as a yellow/brown oil (1.58g, 23%, eluant 4/1 petrol/dichloromethane. Rf= 0.53). (Rf of *p* -toluidine=0.15. Rf values for silica gel, 1/1 petrol/dichloromethane). Recrystallisation of (18) from dichloromethane/ether gave a brown crystalline solid (m.p. 120 - 124.5 °C). This material was a mixture of two diastereoisomers of (18), as evidenced by the 'doubling up' of certain signals in the ^{13}C spectrum:- δH (270MHz) 7.15-7.35 (10H,m,Ar-H); 6.4 5(2H,s,ArC_3-H,ArC_5-H); 4.16 (2H,m,CH); 3.10 (4H,m,CH_2-N); 2.29 (2H,m,CH_2); 2.07 (2H,m,CH_2); 1.98 (3H,s,ArC_4-CH_3). δC (68MHz) 147.36 & 147.48 (Cquat.); 141.36 (ArC_1-N); 129.37 (ArC_3-H, ArC_5-H); 128.88 (ArC-H); 128.40 (ArC-H); 126.15 (ArC-H); 124.90 & 125.13 (ArC_4-CH_3); 123.76 & 123.79 (ArC_2-C,ArC_6-C); 47.51 (CH_2-N); 43.57 & 43.70 (CH); 31.24 & 31.30 (CH_2); 20.41 (ArC_4-CH_3). $\nu_{max.}$($CHCl_3$):- 3075, 3010, 2940, 2870, 2835 1620 ,1607, 1495, 1455 cm^{-1} m/z [Found:- 339.1974 (M^+ 100%); 260(36); 234(14); 220(7); 158(10); 91(($PhCH_2)^+$ 8). $C_{25}H_{25}N$ requires 339.1987].[Found:- C 88.2, H 7.4, N 4.0. $C_{25}H_{25}N$ requires C 88.45, H 7.4, N 4.1%].

Reaction of *p*-toluidine with formaldehyde and 3,4-dihydro-2*H*-pyran

p-Toluidine (1.07g, 10mmol) was dissolved in acetonitrile (14.3ml) containing one equivalent of trifluoroacetic acid(1.14g, 10mmol) to give a 0.7M solution of the amine. This brown solution was added with stirring to a heterogeneous mixture at 0 °C of 3,4-dihydro-2*H*-pyran(4.20g, 50mmol) and 37% formalin solution (4.05ml, 50mmol). The mixture was stirred at room temperature under nitrogen for 30min. and then worked up to give a brown oil (5.92g) which was purified by chromatography on alumina to give the two adducts 6,7,7a,8,10 a,12,13,14a-oct ahydro-2-methyl-3b*H*,5*H*,10*H*,11 *H*-pyrano[3,2-*c*] pyrano[2',3':4, 5]pyrido-[3,2,1 -*ij*]quinoline ((3bα,7aα,10aβ,14aβ)- and (3bα,7aα,10aα, 14aα)- (19) and (20). The less polar which was a cream solid (1.20g, 40%, eluant 2/3 ether/petrol. Rf=0.43) was tentatively assigned structure (20) and the more

polar fraction again a cream solid was assigned structure (19) (1.25g, 42%, eluant 4/1 ether/petrol. Rf=0.28). (Rf of *p* -toluidine=0.39. Rf values for basic alumina, 1/1 ether/petrol). Recrystallisation of (20) from ether gave a cream powder (m.p. 120 - 123 °C). δH(270MHz) 7.00 (2H,s,ArC$_3$-H,ArC$_5$-H); 4.54 (2H,d,J=3.8Hz, CHO); 3.78 (2H,m,CH$_2$-O); 3.64 (2H,m,CH$_2$-O); 3.27 (2H,dd,J=11.1,8.7Hz,CH$_2$-N); 2.96 (2H,dd,J=11.1, 3.7Hz,CH$_2$-N); 2.20 (3H,s,ArC$_4$-CH$_3$); 2.12 (2H,m,CH); 1.48-1.88 (8H,m,CH$_2$). δC (68MHz) 140.37 (ArC$_1$-N); 130.24 (ArC$_3$-H,ArC$_5$-H); 125.59 (ArC$_4$-CH$_3$); 120.80 (ArC$_2$-C,ArC$_6$-C); 73.60 (CHO); 65.54 (CH$_2$-O); 51.13 (CH$_2$-N); 32.19 (CH); 25.08 (CH$_2$); 23.58 (CH$_2$); 20.47 (ArC$_4$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3015, 2950, 2870, 1623, 1503, 1455 cm^{-1}. m/z [Found:- 299.1874 (M$^+$ 84%); 254(6); 240((M-C$_3$H$_7$O)$^+$ 100); 216(4); 195(4); 182 (10); 172(9). $C_{19}H_{25}NO_2$ requires 299.1885].

Recrystallisation of (19) from ether gave white crystals (m.p. 140 - 143 °C) .δH (270MHz) 6.95 (2H,s,ArC$_3$-H, ArC$_5$-H); 4.30 (2H,d,J=3.0Hz,CHO); 3.99 (2H,m,CH$_2$-O); 3.64 (2H,m,CH$_2$-O); 3.45 (2H,dd,J=12.8, 11.6Hz,CH$_2$-N); 2.7 6(2H,m,CH$_2$-N); 2.19 (3H,s,ArC$_4$-CH$_3$); 2.10 (2H,m,CH); 1.37-1.97 (8H,m,CH$_2$). δC(68MHz) 141.03 (ArC$_1$-N); 131.84 (ArC$_3$-H,ArC$_5$-H); 125.71 (ArC$_4$-CH$_3$); 121.85 (ArC$_2$-C,ArC$_6$-C); 74.51 (CHO); 68.30 (CH$_2$-O); 49.45 (CH$_2$-N); 32.74 (CH); 26.10(CH$_2$); 22.47 (CH$_2$); 20.25 (ArC$_4$-CH$_3$). $\nu_{max.}$(CHCl$_3$):- 3010, 2940, 2855, 1627, 1505, 1455 cm^{-1}. m/z [Found:- 299.1872 (M$^+$ 90%); 254(5); 240((M-C$_3$H$_7$O)$^+$ 100); 212(7); 196(5); 182 (11); 172(10). $C_{19}H_{25}NO_2$ requires 299.1885]. [Found:- C 76.1, H 8.3, N 4.6. $C_{19}H_{25}NO_2$ requires C 76.2, H 8.4, N 4.7%].

References

1. Povarov, L. S., *Russ. Chem. Rev.*, **1967**, *36*, 656; Kametani, T.; Takeda, H.; Suzuki, Y.; Kasai, H.; Honda, T., *Heterocycles*, **1986**, *24*, 3385; Cabral, J.; Laszlo, P., *Tetrahedron Lett.*, **1989**, *30*, 7237; Trifonov, L. S.; Orahovats, A. S., *Heterocycles*, **1984**, *22*, 355; Ciufolini, M. A.; Spencer, G. O., *J. Org. Chem.*, **1989**, *54*, 4739; Borrione, E.; Prato, M.; Scorrano, G.; Stivanello, M.; Lucchini, V.; Valle, G., *J. Chem. Soc. Perkin. Trans. 1*, **1989**, 2245; Nomura, Y.; Kimura, M.; Takeuchi, Y.; Tomoda, S.,*Chem. Lett.*, **1978**, 267.
2. Cabral, J.; Laszlo, P.; Montaufier, M. T., *Tetrahedron Lett.*, **1988**, *29*, 547.
3. Lucchini, V; Prato, M.; Scorrano, G.; Tecilla, P., *J. Org. Chem.*, **1988**, *53*, 2251.
4. Kerr, G. H.; Meth-Cohn, O.; Mullock, E. B.; Suschitzky, H, *J. Chem. Soc. Perkin Trans I*, **1974**, 1614.
5. Hesse, K-D, *Liebigs Ann. Chem.*, **1970**, *741*, 117.
6. Grieco, P. A.; Bahsas, A., *Tetrahedron Lett.*, **1988**, *29*, 5855.
7. Gregoire, P. J.; Mellor, J. M.; Merriman, G. D., *Tetrahedron Lett.*, **1991**, *32*, 7099.
8. Mellor, J. M.; Merriman, G. D.; Riviere, P., *Tetrahedron Lett.*, **1991**, *32*, 7103.
9. Shono, T.; Matsumura, Y.; Inoue, K.; Ohmizu, H.; Kashimura, S., *J. Am. Chem. Soc.*, **1982**, *104*, 5733.
10. Swan, G. A., *J. Chem. Soc. Chem. Commun.*, **1969**, 20.
11. Weinreb, S. M.; Scola, P. M., *Chem. Rev.*, **1989**, *89*, 1525; Boger, D. L.; Weinreb, S. M., *'Hetero Diels-Alder Methodology in Organic Synthesis'*, Acadamic Press, San Diego, 1987.
12. Gilchrist, T. L.; Stannard, A-M, *Tetrahedron Lett*, **1988**, *29*, 3585; Kametani, T.; Takeda, H.; Suzuki, Y.; Honda, T., *Synth. Commun.*, **1985**, *15*, 499.
13. Ghosh, A. K.; McKee, S. P.; Sanders, W. M., *Tetrahedron Lett*, **1991**, *32*, 711.
14. Gregoire, P. J.; Mellor, J. M.; Merriman, G. D., *Tetrahedron*, following paper.

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