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Ring-opening Reactions of N-Aryl-1,2,3,4-tetrahydroisoquinoline Derivatives

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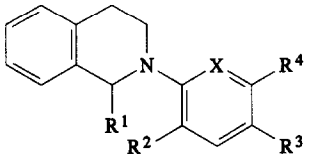
Abstract: The reaction of N-nitroaryl-1,2,3,4-tetrahydroisoquinolines **1a-e,1g** and **1j** with N-bromosuccinimide (NBS) afforded aldehydes **3a-e,3h** and **3j** respectively. N-(4-Nitrophenyl)-1-phenyl-1,2,3,4-tetrahydroisoquinoline **1n** gave ketone **3n** together with brominated product **3o** when treated with NBS.

We have recently described the reaction of nitro-compound **1b** with oxygen which yielded the aldehyde **3b** in 38% yield [1]. We have attributed the preference for aldehyde formation **3b** over formation of the corresponding hemi-aminal **4b** (which was not observed) to intra-molecular hydrogen bonding between the >NH group and the appositely located nitro-group. The presence of hydrogen bonding has recently been confirmed by an X-ray crystallographic investigation of compound **3a** [2].

We were interested in preparing a series of N-(2-nitroaryl)- and N-(4-nitroaryl)-1,2,3,4-tetrahydroisoquinoline derivatives and investigating their ring-opening reactions to establish the preference for either aldehyde and/or hemi-aminal formation. Nitro-compounds **1a-d,1g** and **1j** were readily prepared from tetrahydroisoquinoline and the appropriate chloro- or fluoronitroaryl compound. Nitro-compounds **1l,1m** and **1n** were similarly prepared from 1-methyl-1,2,3,4-tetrahydroisoquinoline or 1-phenyl-1,2,3,4-tetrahydroisoquinoline as appropriate. Compound **1e** was prepared by reaction of 1,2,3,4-tetrahydroisoquinoline with 2,4-difluoronitrobenzene. Besides the required product **1e** (59 %), the isomeric compound **1k** (29 %) was also formed in this reaction and these two products were readily separated by column chromatography. To establish the regioselectivity of nucleophilic substitution in this reaction compound **1e** was reacted with methanolic potassium hydroxide solution giving compound

1f (88 %). Compound **1f** (56 %) was also prepared by reacting 1,2,3,4-tetrahydroisoquinoline with 2-fluoro-4-methoxy-nitrobenzene therefore establishing the structures of these isomers.

	R^1	R^2	R^3	R^4	X
a	H	NO_2	H	H	CH
b	H	NO_2	Me	H	CH
c	H	NO_2	NO_2	H	CH
d	H	NO_2	F	H	CH
e	H	NO_2	H	F	CH
f	H	NO_2	H	OMe	CH
g	H	NO_2	H	H	N
h	H	NO_2	Br	H	N
i	H	H	NO_2	H	CH
j	H	Me	NO_2	H	CH
k	H	H	NO_2	F	CH
l	Me	NO_2	H	H	CH
m	Me	H	NO_2	H	CH
n	Ph	H	NO_2	H	CH
o	Ph	Br	NO_2	H	CH



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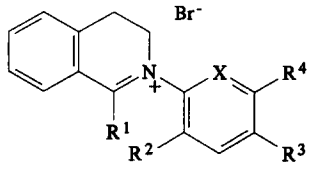

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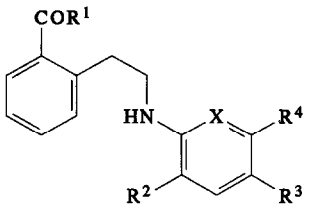

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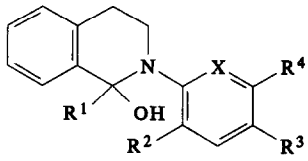

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Ring-opening reactions were achieved by heating the nitro-compounds in either dichloromethane or dichloroethane solution with N-bromosuccinimide (NBS), followed by basic work-up. The reaction of N-aryl-1,2,3,4-tetrahydroisoquinoline derivatives with NBS has only been used occasionally [3] for the preparation of N-aryl-3,4-dihydroisoquinolinium salts: these salts are usually prepared from appropriate aniline derivatives and 2-(2-bromoethyl)benzaldehyde[4].

When compounds **1a-e** were treated with NBS aldehydes **3a-e** respectively were obtained in good yield (84 - 100 %) after basic work-up without isolation of the intermediate N-aryl-3,4-dihydroisoquinolinium salts **2a-e**. Compound **1g** reacted with one equivalent of NBS giving compound **1h** (90 %) where bromination had occurred in the pyridine ring rather than at the 1-position of the tetrahydroisoquinoline ring. With two equivalents of NBS ring-opening was observed and the brominated product **3h** (88 %) was produced. Compound **1h** was also converted into compound **3h** (82 %) by the action of NBS. In all of these ring-opening reactions, only aldehyde products were apparent by ^{1}H-nmr spectroscopy and none of the corresponding hemi-aminals could be detected.

Salt **2a** has previously been prepared from 2-(2-bromoethyl)benzaldehyde and 2-nitroaniline [4] and hydrolysis of this salt gave exclusively the aldehyde **3a** [5] which is in agreement with our observations. Salt **2i** was similarly prepared from 4-nitroaniline and was reported to give only the hemi-aminal **4i** upon hydrolysis [5]. Intra-molecular hydrogen bonding, which undoubtedly contributes to the preference for aldehyde structure **3a**, is not possible in this case.

In contrast to this observation, we have found that compound **1j** gave exclusively the aldehyde **3j** via the salt **2j**. This is presumably due to potentially disfavourable steric interactions that would be present between the methyl-substituent and the hydroxy-group in the corresponding hemi-aminal **4j**.

We were also interested in investigating the ring-opening reactions of the 1-methyl-1,2,3,4-tetrahydroisoquinoline derivatives **1l** and **1m**, anticipating the products **3l** and **3m** respectively. However, when compound **1l** was reacted with NBS a complex mixture was produced possibly due to deprotonation at the methyl group of the resulting iminium salt **2l** yielding an enamine which could undergo further reaction with NBS. In view of this result, reaction of compound **1m** with NBS was not attempted and our attention was turned to the 1-phenyl-1,2,3,4-tetrahydroisoquinoline derivative **1n**. When compound **1n** was reacted with NBS a mixture of two products were obtained and identified as compounds **3n** (39 %) and **3o** (26 %). The less electrophilic and more sterically crowded ketonic carbonyl groups in these products precludes cyclisation to their corresponding hemi-aminals.

Our results presented in this paper clearly indicate that a 2-nitroaryl group will favour aldehyde formation because intra-molecular hydrogen bonding is possible in these cases. When a 4-nitroaryl group is present, intra-molecular hydrogen bonding involving the nitro-group is not possible and other effects dictate whether the aldehyde or hemi-aminal structures are preferred.

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EXPERIMENTAL

Melting points are uncorrected. ^{1}H-nmr spectra (90MHz) were determined in $CDCl_3$ solution unless otherwise stated. Infra-red spectra were recorded as KBr discs unless otherwise stated.

Preparation of Compounds **1a-d,1g,1j** and **1l-n**: General Method.

A mixture of 1,2,3,4-tetrahydroisoquinoline (THIQ) or its 1-methyl or 1-phenyl derivative as appropriate, K_2CO_3 and the appropriate halonitroaryl compound were heated (100°) in DMSO (0.5-2 hr) with stirring. The mixture was poured into water and the product was extracted into dichloromethane (DCM). The organic layer was washed several times with water, dried ($MgSO_4$) and evaporated yielding the product. By this method the following compounds were prepared.

N-(2-Nitrophenyl)-1,2,3,4-tetrahydroisoquinoline **1a**. THIQ (6 g), K_2CO_3 (12.4 g) and 2-fluoronitrobenzene (6.4 g) gave compound **1a** (9.3 g, 81 %) as orange plates, m.p. 100-102° (EtOH) (lit.,[5] not reported). $\nu_{max.}$ 1605, 1510 and 1340 cm^{-1}. δ 7.80 (1H, dd, J 8 and 2 Hz, Ar-H), 7.60-6.75 (7H, m, Ar-H), 4.30 (2H, s, $>CH_2$), 2.95 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 3.40 (2H, t, J 7 Hz, $-CH_2CH_2-$).

N-(4-Methyl-2-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline **1b**. This compound has been described previously [1].

N-(2,4-Dinitrophenyl)-1,2,3,4-tetrahydroisoquinoline **1c**. THIQ (3 g), K_2CO_3 (6.2 g) and 2,4-dinitrochlorobenzene (4.6 g) gave compound **1c** (6.2 g, 92 %) as yellow needles, m.p. 165-168° (acetone). [Found: C,60.45; H,4.35; N,13.9. $C_{15}H_{13}N_3O_4$ requires C,60.2; H,4.4; N,14.0%]. $\nu_{max.}$ 1600, 1500 and 1325 cm^{-1}. δ 8.73 (1H, d, J 3 Hz, Ar-H), 8.34 (1H, dd, J 9 and 3 Hz, Ar-H), 7.25 (5H, m, Ar-H), 4.40 (2H, s, $>CH_2$), 3.61 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 3.05 (2H, t, J 7 Hz,$-CH_2CH_2-$).

N-(2-Nitro-4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline **1d**. THIQ (2.92 g), K_2CO_3 (6.0 g) and 2,5-difluoronitrobenzene (3.5 g) gave compound **1d** (5.0 g, 84%) as red needles, m.p 75-7° (EtOH). [Found: C,65.85; H,4.55; N,10.05. $C_{15}H_{13}FN_2O_2$ requires C,66.15; H,4.82; N,10.3%]. $\nu_{max.}$ 1525 cm^{-1}. δ 7.65-5.95 (7H, m, Ar-H), 4.25 (2H, s, $>CH_2$), 3.35 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 2.99 (2H, t, J 7 Hz, $-CH_2CH_2-$).

N-(3-Nitro-2-pyridyl)-1,2,3,4-tetrahydroisoquinoline **1g**. THIQ (2.0 g), K_2CO_3 (4.1 g) and 2-chloro-3-nitropyridine (2.4 g) gave compound **1g** (3.55 g, 93%) as yellow plates, m.p. 77-8° (EtOH). [Found: M,255.1008. $C_{14}H_{13}N_3O_2$ requires M, 255.1008]. $\nu_{max.}$ 1595 and 1325 cm^{-1}. δ 8.35 (1H, dd, J 5 and 2 Hz, Ar-H), 8.24 (1H, dd, J 8 and 2 Hz, Ar-H), 7.18 (4H, broad s, Ar-H), 6.82 (1H, dd, J 8 and 5 Hz, Ar-H), 4.50 (2H, s, $>CH_2$), 3.75 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 3.00 (2H, t, J 7 Hz, $-CH_2CH_2-$).

N-(2-Methyl-4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline **1j**. THIQ (1.7 g), K_2CO_3 (3.5 g) and 2-fluoro-5-nitrotoluene (2.0 g) gave compound **1j** (1.8 g; 53%) as yellow plates, m.p. 72-75° (EtOH). [Found: C,71.45; H,5.8; N,10.7. $C_{16}H_{16}N_2O_2$ requires C,71.6; H,6.0; N,10.45%]. $\nu_{max.}$ 1500

and 1330 cm^{-1}. δ 8.10 (2H, m, Ar-H), 7.18 (5H, m, Ar-H), 4.29 (2H, s, $>CH_2$), 3.48 (2H, t, J 7 Hz, $-CH_2CH_2-$), 3.04 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 2.38 (3H, s, Ar-Me).

N-(2-Nitrophenyl)-1-methyl-1,2,3,4-tetrahydroisoquinoline **11**. 1-Methyl-1,2,3,4-tetrahydroisoquinoline (3.0 g), K_2CO_3 (5.48 g) and 2-fluoronitrobenzene (2.9 g) gave compound **11** (5.15 g, 96%) as orange plates, m.p. 86-88° (EtOH). [Found: C,71.3; H,5.95; N,10.3. $C_{16}H_{16}N_2O_2$ requires C,71.6; H,6.0; N,10.4%]. $V_{max.}$ 1525, 1480 and 1370 cm^{-1}. δ 7.70 (1H, dd, J 8 and 2 Hz, Ar-H), 7.54-6.90 (7H, m, Ar-H), 4.65 (1H, q, J 7 Hz, Me-CH<), 3.32 (2H, m, $-CH_2CH_2-$), 2.80 (2H, m, $-CH_2CH_2-$) and 1.40 (3H, d, J 7 Hz, -Me).

N-(4-Nitrophenyl)-1-methyl-1,2,3,4-tetrahydroisoquinoline **1m**. 1-Methyl-1,2,3,4-tetrahydroisoquinoline (0.35 g), K_2CO_3 (0.64 g) and 4-fluoronitrobenzene (0.34 g) gave compound **1m** (0.50 g, 77%) as orange needles, m.p. 109-110° (EtOH). [Found: C,71.35; H,5.85; N,10.25. $C_{16}H_{16}N_2O_2$ requires C,71.6; H,6.0; N,10.4%]. $V_{max.}$ 1590, 1480, 1305 and 1110 cm^{-1}. δ 8.15 (2H, d, J 9 Hz, Ar-H), 7.24 (4H, m, Ar-H), 6.80 (2H, d, J 9 Hz, Ar-H), 5.00 (1H, q, J 7 Hz, MeCH<), 3.69 (2H, t, J 7 Hz, $-CH_2CH_2-$), 3.03 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 1.54 (3H, d, J 7 Hz, -Me).

N-(4-Nitrophenyl)-1-phenyl-1,2,3,4-tetrahydroisoquinoline **1n**. 1-Phenyl-1,2,3,4-tetrahydroisoquinoline (0.5 g), K_2CO_3 (0.65 g) and 1-fluoro-4-nitrobenzene (0.34 g) gave compound **1n** (0.71 g, 90%) as yellow leaves, m.p. 145-147° (EtOH). [Found: C,76.15; H,5.3; N,8.55. $C_{21}H_{18}N_2O_2$ requires C,76.3; H,5.5; N,8.5%]. $V_{max.}$ 1595, 1480 and 1320 cm^{-1}. δ 8.12 (2H, d, J 9 Hz, Ar-H), 7.45-7.00 (9H, m, Ar-H), 6.77 (2H, d, J 9 Hz) 5.95 (1H, s, >CH-), 4.00-3.40 (2H, m, $-CH_2CH_2-$) and 2.95 (2H, broad m, $-CH_2CH_2-$).

Preparation of N-(2-Nitro-5-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline **1e** and N-(3-Fluoro-4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline **1k**. THIQ (2.60 g) was added dropwise (5 min.) to a cooled (ice-bath), stirred mixture of 2,4-difluoro- nitrobenzene (3.20 g) and K_2CO_3 (4.0 g) in dimethylformamide (DMF) (10 ml). The mixture was stirred in the cold and then allowed to warm to room temperature. After stirring overnight, the mixture was poured into water and extracted with DCM. The organic layer was washed with water, dried ($MgSO_4$) and evaporated yielding an orange oil (4.67 g, 88%) which was shown to be a 2:1 mixture of the title compounds by ^{1}H-nmr spectroscopy. This oil was fractionated by column chromatography (silica gel, eluent petroleum ether b.p. 60-80°: ethyl acetate 9:1) giving compound **1e** as yellow plates, m.p. 84-85° (EtOH). [Found: C,66.1; H,4.6;

N,10.4. $C_{15}H_{13}FN_2O_2$ requires C,66.2; H,4.8; N,10.3%]. $V_{max.}$ 1620, 1570, 1515, 1345 and 1250 cm^{-1}. δ 7.88 (1H, dd, J 7 and 10 Hz, Ar-H), 7.18 (4H, broad s, Ar-H), 6.82 (1H, dd, J 12 and 2 Hz, Ar-H), 6.60 (1H, td, J 10 and 2 Hz, Ar-H), 4.28 (2H, s, $>CH_2$), 3.40 (2H, t, J 6 Hz, $-CH_2CH_2-$) and 3.00 (2H, t, J 6 Hz, $-CH_2CH_2-$). The eluent was then changed to petroleum ether b.p. 60-80°: ethyl acetate 8:2 giving compound **1k** as yellow plates, m.p. 125-7° (EtOH). [Found: C,66.4; H,4.75; N,10.5. $C_{15}H_{13}FN_2O_2$ requires C,66.2; H,4.8; N,10.3%]. $V_{max.}$ 1610, 1580 and 1320 cm^{-1}. δ 8.02 (1H, t, J 10 Hz, Ar-H), 7.21 (4H, broad s, Ar-H), 6.70-6.30 (2H, m, Ar-H), 4.50 (2H, s, $>CH_2$), 3.66 (2H, t, J 6 Hz, $-CH_2CH_2-$) and 3.00 (2H, t, J 6 Hz, $-CH_2CH_2-$).

Preparation of N-(2-Nitro-5-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline **1f**. Method A. A solution of compound **1e** (0.13 g) and potassium hydroxide (0.10 g) in methanol (4 ml) was heated at reflux (0.75 hr), allowed to cool to room temperature and then evaporated. Water was added to the residue and the mixture was extracted with DCM. The organic layer was washed with water, dried ($MgSO_4$) and evaporated giving compound **1f** (0.12 g, 88%) as an orange oil which slowly crystallised giving a waxy solid, m.p. 48-50°. [Found: C,67.75; H,5.5; N,9.75. $C_{16}H_{16}N_2O_3$ requires C,67.6; H,5.7; N,9.85%]. $V_{max.}$ 1610, 1570 and 1500 cm^{-1}. δ 7.98 (1H, d, J 9 Hz, Ar-H), 7.12 (4H, broad s, Ar-H), 6.65-6.30 (2H, m, Ar-H), 4.26 (2H, s, $>CH_2$), 3.82 (3H, s, -OMe), 3.38 (2H, broad t, J 6 Hz, $-CH_2CH_2-$) and 3.00 (2H, broad t, $-CH_2CH_2-$). Method B. A mixture of THIQ (0.27 g), 2-fluoro-4-methoxynitrobenzene [6] (0.34 g) and K_2CO_3 (0.60 g) in DMSO (4 ml) was heated (2.5 hr) at 100° with stirring and then poured into water. The mixture was extracted with DCM and the organic layer was washed with water, dried ($MgSO_4$) and evaporated giving compound **1f** (0.32 g, 56%), identical with an authentic sample.

Preparation of N-[6-(3-Bromo-5-nitropyridyl)]-1,2,3,4-tetrahydroisoquinoline **1h**. Compound **1g** (0.25 g), NBS (0.17 g) and a few crystals of dibenzoylperoxide were heated (3 hr) at reflux in 1,2-dichloroethane (DCE) (25 ml). After cooling to room temperature, the mixture was washed with dilute sodium hydroxide solution and then with water, dried ($MgSO_4$) and evaporated giving compound **1h** (0.30 g, 90%) as yellow plates, m.p. 112-114° (EtOH). [Found: C,50.6; H,3.55; Br,23.75; N,12.9. $C_{14}H_{12}BrN_3O_2$ requires C,50.3; H,3.6; Br,23.9; N,12.6%]. $V_{max.}$ 1595 cm^{-1}. δ 8.38 (2H, m, Ar-H), 7.18 (4H, m, Ar-H), 4.43 (2H, s, $>CH_2$), 3.42 (2H, t, J 7Hz, $-CH_2CH_2-$) and 2.99 (2H, t, J 7 Hz, $-CH_2CH_2-$).

Preparation of Aldehydes **3a-e,3h** and **3j** and of Ketones **3n** and **3o**: General

Method. A mixture of the appropriate nitro-compound, NBS and a few crystals of dibenzoylperoxide were heated at reflux (1-2 hr) in DCM or DCE. After cooling to room temperature, the mixture was washed with dilute sodium hydroxide solution and then with water, dried ($MgSO_4$) and evaporated giving the product(s). By this method the following compounds were prepared.

N-(2-Nitrophenyl)-2-(2-aminoethyl)benzaldehyde **3a**. Compound **1a** (0.25 g) and NBS (0.18 g) in DCM gave aldehyde **3a** (0.25 g, 95 %) as orange needles, m.p. 97-99° (EtOH), (lit.,[5] not reported). $\nu_{max.}$ 3370, 1690, 1615, 1570 and 1510 cm^{-1}. δ 10.15 (1H, s, -CHO), 8.15 (2H, d, J 8 Hz, Ar-H), 7.95-7.25 (5H, m, Ar-H + >NH), 6.95 (1H, d, J 8 Hz, Ar-H), 6.65 (1H, m, Ar-H) and 3.52 (4H, m, $-CH_2CH_2-$). Compound **3a** formed a 2,4-dinitrophenylhydrazone derivative, m.p. 237-239°. [Found: C,56.0; H,4.0; N,18.95. $C_{21}H_{17}N_6O_6$ requires C,56.1; H,3.8; N,18.7%].

N-(4-Methyl-2-nitrophenyl)-2-(2-aminoethyl)benzaldehyde **3b**. Compound **1b** (0.25 g) and NBS (0.17 g) in DCM gave aldehyde **3b** (0.26 g, 98%), identical with an authentic sample [1].

N-(2,4-Dinitrophenyl)-2-(2-aminoethyl)benzaldehyde **3c**. Compound **1c** (0.25 g) and NBS (0.15 g) in DCE gave aldehyde **3c** (0.22 g, 84%) as yellow needles, m.p. 183-185° (acetone). [Found: C,60.45; H,4.35; N,13.9. $C_{15}H_{13}N_3O_4$ requires C,60.2; H,4.4; N,14.0%]. $\nu_{max.}$ 3330, 1680, 1620, 1585, 1520, 1410, 1330, 1300 and 1235 cm^{-1}. δ 10.10 (1H, s, -CHO, 9.10 (1H, d, J 3 Hz, Ar-H), 8.67 (1H, broad s, >NH), 8.26 (1H, dd, J 10 and 3 Hz, Ar-H), 7.90-7.05 (5H, m, Ar-H) and 3.85-3.30 (4H, m, $-CH_2CH_2-$).

N-(2-Nitro-4-fluorophenyl)-2-(2-aminoethyl)benzaldehyde **3d**. Compound **1d** (0.5 g) and NBS (0.33 g) in DCM gave compound **3d** (0.49 g, 92%) as orange plates, m.p 130-132° (EtOH). [Found: C,62.45; H,4.55; N,9.9. $C_{15}H_{13}FN_2O_3$ requires C,62.5; H,4.55; N,9.7%]. $\nu_{max.}$ 3370, 1690 and 1520 cm^{-1}. δ 10.13 (1H, s, -CHO), 8.05 (1H, broad s, >NH), 7.95-6.90 (7H, m, Ar-H) and 3.50 (4H, m, $-CH_2CH_2-$).

N-(2-Nitro-5-fluorophenyl)-2-(2-aminoethyl)benzaldehyde **3e**. Compound **1e** (0.27 g) and NBS (0.18 g) in DCM gave compound **3e** (0.28 g, 100%) as bright yellow needles, m.p. 125° (EtOH). [Found: C,62.4; H,4.4; N,9.75. $C_{15}H_{13}FN_2O_3$ requires C,62.5; H,4.55; N,9.7%]. $\nu_{max.}$ 3380, 1690, 1630, 1570 and 1505 cm^{-1}. δ 10.10 (1H, s, -CHO), 8.18 (2H, broad dd, J 10 and 6 Hz, Ar-H and >NH), 7.90-7.20 (4H, m, Ar-H), 6.63 (1H, dd, J 11 and 2 Hz), 6.30 (1H, td, J 11 and 2 Hz, Ar-H), and 3.48 (4H, m, $-CH_2CH_2-$).

N-[6-(3-Bromo-5-Nitropyridyl)]-2-(2-aminoethyl)benzaldehyde **3h**. Method A. Compound **1g** (0.25 g) and NBS (0.35 g) in DCE gave compound **3h** (0.31 g 88%) as bright yellow leaves, m.p. 169-171° (EtOH). [Found: C,48.5; H,3.45; Br,22.4; N,12.0. $C_{14}H_{12}BrN_3O_2$ requires C,48.0; H,3.45;

Br,22.8; N,12.0%]. $V_{max.}$ 3325, 1670, 1600, 1560 and 1210 cm^{-1}. δ 10.23 (1H, s, -CHO), 8.48 (2H, d, J 7 Hz, Ar-H), 7.84 (1H, m, Ar-H), 7.38 (3H, m, Ar-H), 3.86 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 3.48 (2H, t, J 7 Hz, $-CH_2CH_2-$). Method B. Compound **1h** (0.05 g) and NBS in DCE gave compound **3h** (0.04 g, 82%).

N-(2-Methyl-4-nitrophenyl)-2-(2-aminoethyl)benzaldehye **3j**. Compound **1j** (1.0 g) and NBS (0.68 g) in DCM (25 ml) gave a precipitate [1.12 g, 87% (salt **2j**)] which was collected. This solid (0.6 g) was partitioned between dilute sodium hydroxide solution and DCM. Compound **3j** (0.45 g, 92%) was isolated from the organic layer as yellow plates, m.p. 133-134° (EtOH). [Found: C,67.65; H,5.65; N,9.9. $C_{16}H_{16}N_2O_3$ requires C,67.6; H,5.7; N,9.9%]. $V_{max.}$ 3380, 1695, 1680, 1600, 1585, 1530, 1480, 1320 and 1285 cm^{-1}. δ 10.16 (1H, s, -CHO), 8.15-7.70 (3H, m, Ar-H), 7.70-7.20 (3H, m, Ar-H), 6.55 (1H, d, J 8 Hz, Ar-H), 4.84 (1H, broad s, >NH), 3.75-3.25 (4H, m, $-CH_2CH_2-$) and 2.10 (3H, s, -Me).
N-(2-Methyl-4-nitrophenyl)-3,4-dihydroisoquinolinium Bromide **2j**: m.p. 247-249°. $V_{max.}$ 1620, 1560, 1510 and 1335 cm^{-1}. δ (d_6-DMSO) 9.63 (1H, s, iminium-H), 8.55-7.50 (7H, m, Ar-H), 4.48 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 2.77-2.35 (5H, m, $-CH_2CH_2-$ and overlapping -Me).

N-(4-Nitrophenyl)-2-(2-aminoethyl)benzophenone **3n** and N-(2-Bromo-4-nitrophenyl)-2-(2-aminoethyl)benzophenone **3o**. Compound **1n** (0.30 g) and NBS (0.32 g) in DCM gave, after chromatography (silica gel, eluent petroleum ether b.p 60-80°: ethyl acetate 9:1) ketone **3n** (0.12 g, 39%) and ketone **3o** (0.10 g, 26%). Ketone **3n**: orange oil. $V_{max.}$ 3385, 1660, 1600, 1310 (broad) and 1100 cm^{-1}. [Found: M, 347.1396. $C_{21}H_{19}N_2O_3$ (M+H) requires M, 347.1396]. δ 8.00 (2H, d, J 10 Hz, Ar-H), 7.82 (2H, dd, J 8 and 2 Hz, Ar-H), 7.45 (7H, m, Ar-H), 6.45 (2H, d, J 10 Hz, Ar-H), 6.05 (1H, broad s, >NH), 3.50 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 2.95 (2H, t, J 7 Hz, $-CH_2CH_2-$). Ketone **3o**: yellow plates, m.p. 88-90° (EtOH). [Found: C,59.0; H,3.8; N,6.45. $C_{21}H_{17}N_2O_3Br$ requires C,59.3; H,4.0; N,6.6%]. $V_{max.}$ 3385, 1660, 1590, 1295 (broad) and 1115 cm^{-1}. δ 8.25 (1H, d, J 2 Hz, Ar-H), 8.02 (1H, dd, J 8 and 2 Hz, Ar-H), 7.81 (2H, d, J 8 Hz, Ar-H), 7.66-7.20 (7H, m, Ar-H), 6.55 (1H, d, J 10 Hz, Ar-H), 5.90-5.40 (1H, broad s, >NH), 3.60 (2H, t, J 7 Hz, $-CH_2CH_2-$) and 3.05 (2H, t, J 7 Hz, $-CH_2CH_2-$).

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