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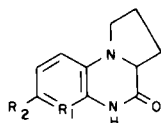
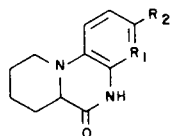
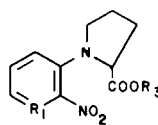
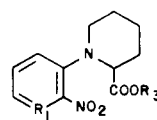
1,2,3,3a-Tetrahydro-9-nitropyrrolo[1,2-*a*]quinoxalin-4-one and 7,8,9,10-tetrahydro-3-nitropyrido[1,2-*a*]quinoxalin-6-one (V-VI) were reduced and deaminated to give new parent tricyclic quinoxalinone skeletons I-II. The latter compounds were identical with the tricycles obtained by an unambiguous independent synthesis. New 6-aza-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]quinoxalin-4-one (III) and 4-aza-7,8,9,10-tetrahydropyrrolo[1,2-*a*]quinoxalin-6-one (IV) were prepared by selective hydrogen transfer reductive cyclisation of esters of *N*-(2-nitro-3-pyridyl)pyrrolidine-2-carboxylic acid and *N*-(2-nitro-3-pyridyl)piperidine-2-carboxylic acid (Xb and XIb) respectively.

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In continuation of our interest on synthesis and chemistry of new heterocyclic quinoxalinones with bridge-head nitrogen atoms and a fully-reduced ring C [1] and following our earlier observation [1] that derivatives of *N*-(2-nitrophenyl)cycloamine-2-carboxylates cyclise readily under selective hydrogen transfer reduction conditions to give the corresponding tricyclic quinoxalinones, we have presently investigated the utility of this new route to a general synthesis of the parent skeleton as well as the 4 or 6-azatricyclic quinoxalinones.

Deamination of aminobenzenes has been quite well explored as a route to unsubstituted benzenes [2]. We report here the successful transformation of the nitro derivatives of the tricyclic quinoxalinones into the parent compounds. The spectroscopic properties of the parent compounds agree well with the data obtained for tricycles resulting from cyclisation of *N*-(2-nitrophenyl)cycloamine-2-carboxylates.

As far as we know, the only tricyclic azaquinoxalinone reported is a chelidamic acid derivative obtained by treatment of diethyl chelidonate with 2,3-diaminopyridine [3]. Bicyclic azaquinoxalinones (pyrido[2,3-*b*]pyrazines) are however available commercially. In fact, recently these bicyclic azaquinoxalinones were used as synthons for Reissert compound studies [4] as a follow-up to the earlier use of the tricyclic pyrrolo[1,2-*a*]quinoxalinones [5]. This situation prompted us to explore the possibility of preparing new 4 or 6-azaheterotricyclic quinoxalinones (*e.g.* III and IV) *via* our hydrogen transfer reductive cyclisation routes.

I $R_1 = -CH-$, $R_2 = H$ III $R_1 = -N-$, $R_2 = H$ V $R_1 = -CH-$, $R_2 = NO_2$ VII $R_1 = -CH-$, $R_2 = NH_2$ II $R_1 = -CH-$, $R_2 = H$ IV $R_1 = -N-$, $R_2 = H$ VI $R_1 = -CH-$, $R_2 = NO_2$ VIII $R_1 = -CH-$, $R_2 = NH_2$ IX a $R_1 = -CH-$, $R_3 = H$ b $R_1 = -CH-$, $R_3 = -CH_3$ XI a $R_1 = -N-$, $R_3 = H$ b $R_1 = -N-$, $R_3 = CH_3$ X a $R_1 = -CH-$, $R_3 = H$ b $R_1 = -CH-$, $R_3 = CH_3$ XII a $R_1 = -N-$, $R_3 = H$ b $R_1 = -N-$, $R_3 = CH_3$

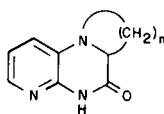
Treatment of the nitroesters IXb and Xb as usual with 10% palladium on charcoal in refluxing ethanol and cyclohexene gave the parent tricyclic quinoxalinones I and II in good yield. The nitroester precursors were obtained only by condensation of the cycloaminocarboxylic acids with 1-fluoro-2-nitrobenzene followed by methylation of the adducts IXa and Xa. Attempts with bromo or chloronitrobenzene were either unsuccessful or gave poor yields.

The micro analysis, ir and pmr data utilized in assigning structures to these parent compounds were also identical to those obtained after reduction and deamination of the nitro analogues earlier obtained [1].

Starting with 3-chloro-2-nitropyridine (obtained by phosphorus oxychloride treatment of the corresponding pyridinol) and condensing it with the appropriate cycloamine carboxylic acid (pyrrolidine-2-carboxylic acid or piperidine-2-carboxylic acid) in dilute bicarbonate solutions [1], the new adducts XIa and XIIa were obtained in good yields. These were converted to the nitropyridine esters XIb and XIIb. Catalytic hydrogen transfer reduction of the nitroesters [6] in the usual manner [1] gave the corresponding *N*-(2-aminopyridine) compounds which were cyclised immediately to the azaquinoxalinones III and IV.

The structures of all the new compounds prepared were assigned by elemental analyses and spectral data. Spectroscopic properties of the tricyclic quinoxalinones have been discussed earlier [1]. However the spectral properties for the 4 or 6-aza compounds are outlined on the table.

Table
Spectroscopic Properties of Tricyclic Azaquinoxalinone Derivatives



Compound No.	Mp (°C)	¹ H-NMR δ	ν max, cm ⁻¹	ms (% RI)
III (n = 3)	175-176	1.9 (4H, m)	3480 (N-H)	188.98 (100)
		3.8 (2H, m)	1680 (C=O)	160.97 (30)
		4.1 (1H, m)		144.96 (92)
		6.0 (aromatic 2H, m)	750	133 (42)
		7.3-8.0 (aromatic 2H, m) 9.56 (exchangeable 1H)		
IV (n = 4)	oil	1.6 (6H, m)	3300 (N-H)	202.96 (100)
		4.0 (2H, m)	1675 (C=O)	175 (28)
		4.2 (1H, m)	750	158.96 (89)
		6.0 (aromatic, 1H)		144 (45)
		7.2-7.4 (2H, m) 9.80 (exchangeable H)		

EXPERIMENTAL

Melting points were determined with a Kofler hot plate apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer 257 Spectrophotometer using Nujol mulls or potassium bromide discs. The pmr spectra were determined on a Varian 60 MHz instrument using pyridine-d₅ solutions (unless otherwise stated) with TMS as an internal standard. The mass spectra were obtained at 70 eV. Microanalyses were partly done at the Microanalytical Laboratory of the School of Chemistry, University of Bristol, Bristol, England.

N-(2-Nitrophenyl)cycloamine-2-carboxylic Acids IXa, Xa.

These compounds were obtained by refluxing 1:1.5 molar ratios of 1-fluoro-2-nitrobenzene in ethanol and the appropriate cycloamine carboxylic acid (L-proline or pipercolinic acid) in sodium hydrogen carbonate for 5 hours. The basic solution in each case was allowed to cool and washed by extraction with chloroform. The aqueous layer was acidified (2*M* hydrochloric acid) and the resulting oil was taken up in chloroform and dried over anhydrous magnesium sulphate. After removal of solvents, a residue was obtained in each case.

Compound IXa.

This compound was obtained as a yellow oil (60%); ir: 2950 (OH), 1700 (C=O), 1610 (s), 1560 (NO₂), 740 (s) cm⁻¹; nmr (deuteriochloroform): δ 2.4 (4H, m, pyrrolidine), 3.5 (2H, m), 4.5 (1H, t), 6.9 and 7.1 (2 singlets, aromatic, 2H), 7.4 (1H, ArH), 7.8 (1H, d, J = 8 Hz), 9.0 (1H, s, exchangeable with deuterium oxide).

Anal. Calcd. for C₁₁H₁₂N₂O₄: C, 55.93; H, 5.08; N, 11.86. Found: C, 55.52; H, 5.32; N, 11.90.

Compound Xa.

The product was obtained as a yellow residue which crystallised from petroleum ether (40-60°) as yellow prisms (60%) mp 78-80°; ir: 3000 (OH), 1710 (C=O), 1600, 1520 (NO₂), 750 (s) cm⁻¹; nmr (deuteriochloroform): δ 1.8 (4H, piperidine), 2.2 (2H, m), 3.0-3.6 (2H, m), 4.2 (1H, t), 7.0 and 7.4 (aromatic 2H, m), 7.6 (1H, m, ArH), 7.8 (1H, d, J = 8 Hz), 10.0 (1H, s, exchangeable OH).

Anal. Calcd. for C₁₂H₁₄N₂O₄: C, 57.60; H, 5.60; N, 11.20. Found: C,

57.40; H, 5.99; N, 11.31.

Methyl *N*-(2-Nitrophenyl)cycloamine-2-carboxylates IXb, Xb.

These compounds were similarly obtained by refluxing the appropriate carboxylic acid, IXa or Xa, with anhydrous methanol containing concentrated sulphuric acid followed by the usual workup as previously reported [1].

Compound IXb.

The product was recrystallised from diethyl ether-petroleum ether (40-60°) giving yellow crystals (90%), mp 77-78°; ir: 1750 (s), (C=O), 1600 (s), 1510 (NO₂), 1350 (C-O), 750 cm⁻¹; nmr δ 2.2 (4H, m, pyrrolidine), 3.4 (2H, m), 3.9 (s, OCH₃), 4.7 (1H, m), 7.0 and 7.2 (2 singlets, aromatic, 2H), 7.6 (1H, m, ArH), 7.8 (1H, d, J = 8 Hz); ms: 249.89, (M⁺, 5.2%), 90.92 (M⁺ - 59, 100%).

Anal. Calcd. for C₁₂H₁₄N₂O₄: C, 57.60; H, 5.60; N, 11.20. Found: C, 57.68; H, 5.68; N, 11.14.

Compound Xb.

The product was obtained as a thick transparent yellow oil (95%); ir: 1740 (C=O), 1600 (s), 1520 (NO₂), 1340 (C-O), 750 cm⁻¹; nmr (deuteriochloroform): δ 1.8 and 2.0 (6H, m, piperidine), 3.2 (2H, m), 3.9 (s, OCH₃), 4.2 (1H, t), 7.0 to 7.4 (aromatic 2H, m), 7.6 (1H, m, ArH), 7.8 (1H, d, J = 8 Hz); ms: 263.95 (M⁺, 5.8%), 205 (M⁺ - 59, 100%).

Anal. Calcd. for C₁₃H₁₆N₂O₄: C, 59.09; H, 6.06; N, 10.61. Found: C, 58.85; H, 6.15; N, 10.55.

N-(2-Nitro-3-pyridyl)cycloamine-2-carboxylic Acids XIa, XIIa.

The appropriate cycloamine-2-carboxylic acid (L-proline or pipercolinic acid) (3.5 mmoles) in sodium hydrogen carbonate was refluxed with 2-chloro-3-nitropyridine (2.4 mmoles) in ethanol for 5 hours. The experiment in each case was carried out and worked up as described for *N*-(2-nitrophenyl)cycloamine-2-carboxylic acids above.

Compound XIa.

The product was recrystallised from diethyl ether-petroleum ether (40-60°), to give light green plates (53%) mp 137-138°; ir: 1705 (C=O), 1595 (s), 1375, 750 cm⁻¹; nmr (deuteriochloroform); δ 1.4 (4H, m, pyrrolidine), 2.4 (2H, m), 4.0 (1H, m), 6.0 (1H, aromatic, q, J = 6 Hz, and J_{5,6}

= 4 Hz), 7.45 (aromatic 1H, dd, $J = 8$ Hz and $J = 2.0$ Hz), 7.6 (1H, ArH, dd, $J = 6$ Hz and $J = 2.0$ Hz), 9.0 (1H, s, exchangeable with deuterium oxide).

Anal. Calcd. for $C_{10}H_{11}N_3O_4$: C, 50.63; H, 4.64; N, 17.72. Found: C, 50.40; H, 4.91; N, 17.55.

Compound XIIa.

The product was a light yellow oil (55%); ir: 1705 (C=O), 1595 (s), 1550, 1320, 750 cm^{-1} ; nmr: δ 1.0 (4H, m, piperidine), 1.6 (2H, m), 2.9 (2H, m), 4.2 (1H, m), 6.0 (aromatic 1H, q, $J = 6$ Hz and 4 Hz), 7.2 (1H, aromatic, dd, $J = 8$ Hz and 2.0 Hz), 7.4 (1H, dd, $J = 6$ Hz and 2.0 Hz), 9.2 (1H, s, OH).

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 50.57; H, 5.18; N, 16.73. Found: C, 50.66; H, 5.46; N, 16.51.

Methyl *N*-(2-Nitro-3-pyridyl)cycloamine-2-carboxylates XIb, XIIb.

A mixture of the appropriate carboxylic acid, Xa or XIa, (9 mmoles) was dissolved in anhydrous methanol (100 ml) containing concentrated sulphuric acid (1.5 ml). The solution was refluxed for 8 hours. The reactions were worked up as previously described [1].

Compound XIb.

The product melted at 86-88°; ir: 1740 (C=O), 1595 (s), 1210 (s), 750 cm^{-1} ; nmr (deuteriochloroform): δ 1.4 (4H, m), 2.4 (2H, m), 3.8 (s, OCH₃), 4.6 (1H, t), 6.0 (1H, ArH, q), 7.45 (1H, aromatic, dd), 7.6 (1H, ArH, dd).

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 50.57; H, 5.18; N, 16.73. Found: C, 50.40; H, 5.15; N, 16.74.

Compound XIIb.

The product was a yellowish green oil (80% yield); ir: 1740 (C=O), 1595 (s), 1205 (s), 760 cm^{-1} ; nmr: δ 1.0 (4H, m, piperidine), 1.6 (2H, m), 2.9 (2H, m), 3.8 (s, OCH₃), 4.2 (1H, m), 6.0 (aromatic 1H, q, $J = 6$ Hz and 4 Hz), 7.2 (1H, aromatic, dd, $J = 8$ Hz and 2.0 Hz), 7.4 (1H, dd); ms: 264.97 (M^+ , 6.5%), 206.15 ($M^+ - 59$, 100%).

Anal. Calcd. for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.66; N, 15.84. Found: C, 54.30; H, 5.58; N, 15.82.

Tricyclic Quinoxalin-4-ones I and II. (a) General Reduction and Deamination Procedure.

To the appropriate nitroquinoxaline tricyclic compound, V or VI, (4.3 mmoles) was added granulated tin (3 g). Concentrated hydrochloric acid (10 ml) was added in three equal portions to the mixture before refluxing for 25 to 30 minutes. There was a colour change from dark brown to light red. The solution was filtered and the filtrate was treated with 2% sodium hydroxide until the precipitate initially formed dissolved. The resulting solution was extracted thrice with diethyl ether and the organic layer was washed with water until the washings were neutral to litmus, dried over anhydrous magnesium sulphate. After removal of the ether, the residue in each case crystallised from petroleum ether to give compounds VII and VIII as shiny light brown prisms respectively with melting points, tlc, nmr and ir characteristics different from the starting compounds.

Compound VII.

This was obtained as shiny light brown prisms (65%) mp 197-198°; ir: 3200 (s, N-H), 1670, 750 cm^{-1} ; nmr (DMSO- d_6): δ 2.2 (4H, m), 3.4 (2H, m), 4.7 (1H, t), 6.0 (1H, ArH), 6.4 (1H, dd), 6.6 (1H, d), 8.8 (2H, broad, exchangeable with deuterium oxide), 9.5 (1H, s).

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 64.71; H, 6.37; N, 20.58. Found: C, 64.75; H, 6.60; N, 20.18.

Compound VIII.

This was also obtained as light brown microcrystalline product (70%) mp 180-182°; ir: 3250 (s, N-H), 1680, 740 cm^{-1} ; nmr (DMSO- d_6): δ 1.8 (6H, m, piperidine), 2.4 (2H, m), 3.4 (2H, m), 4.0 (1H, m), 6.2 (2H, ArH), 6.4 (1H, ArH), 6.6 (1H, ArH), 9.5 (1H, s), 10.3 (2H, broad, exchangeable with deuterium oxide).

Anal. Calcd. for $C_{12}H_{15}N_3O$: C, 66.36; H, 6.91; N, 19.35. Found: C,

66.41; H, 6.60; N, 19.05.

Deamination.

Concentrated sulphuric acid (7 ml) was cooled to -10° before sodium nitrite (0.012 mole) was gradually added with vigorous stirring. Brown fumes of nitrogen dioxide was evolved instantly. After complete addition of the nitrite, the acid solution was warmed to 70° when a clear solution resulted. The solution was cooled to -10° before a solution of each of the amine above (2.5 mmoles) in glacial acetic acid (12 ml) was added gradually. After stirring for $\frac{1}{2}$ hour, copper powder (0.83 g) was added. The mixture was heated for 2 hours. The filtrate was extracted with chloroform thrice. The organic layer was dried over anhydrous magnesium sulphate. On evaporation of solvents, a residue which crystallised on standing was obtained (48%). The elemental analyses and spectral properties of the compounds obtained were identical in all respects with those of compounds I and II and are described below.

(b) General Direct Cyclisation Procedure.

To *N*-(2-nitrophenyl)cycloamine-2-carboxylic acid methyl ester IXb or Xb, (2.0 g, 8 mmoles) was added dried and redistilled cyclohexene (4 ml, 50 mmoles) and 10% palladium on charcoal (5 g) with absolute ethanol (50 ml). The mixture was heated under reflux for 2 hours. The dark mixture was filtered through celite after which the solvents were completely removed leaving a gum.

Compound I.

The gum crystallized from *n*-hexane to give a brown crystalline product, 700 mg (62%), mp 174-175°; ir: 3400 (N-H), 1655 (lactam C=O), 740 cm^{-1} ; nmr: δ 2.0 (pyrrolidine 4H, m), 3.9 (2H, m), 4.1 (1H, m), 6.8-7.0 (aromatic 4H, m), 9.87 (broad -NH); ms: 187.93 (M^+ , 100%), 160 ($M^+ - 28$, 32%), 131.97 (96%).

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.21; H, 6.38; N, 14.89. Found: C, 70.37; H, 6.11; N, 14.83.

Compound II.

The gum was crystallised from *n*-hexane-benzene mixture to give brown prisms (900 mg, 59%), mp 148-149°; ir: 3400 (m), 1675 (s), (lactam C=O), 1205 (s), 750 cm^{-1} ; nmr: δ 1.9 (6H, m, piperidine), 3.9 (2H, m), 4.0 (1H, m), 7.0 (4H, aromatic, s, broad at base), 9.08 (1H, broad, exchangeable with deuterium oxide); ms: 201.89 (M^+ , 100%), 173.86 ($M^+ - 28$, 33%), 147 (96%).

Anal. Calcd. for $C_{12}H_{14}N_2O$: C, 71.29; H, 6.93; N, 13.86. Found: C, 71.32; H, 6.64; N, 13.70.

6-Aza-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]quinoxalin-4-one (III).

Absolute ethanol (200 ml) was added to a mixture of methyl *N*-(2-nitro-3-pyridyl)pyrrolidine-2-carboxylate (2 g, 8 mmoles) and dried cyclohexene (4 ml, 50 mmoles) containing 10% palladium-on-charcoal (5 g). The mixture was heated under reflux for 2 hours. The greenish mixture was filtered after which the solvents were completely removed to leave a light brown gum which crystallised on standing to give an off-white crystalline product 400 mg (51%), mp 175-176°; ir: 3100 (s), 1680 (s) (lactam C=O), 750 cm^{-1} ; nmr: δ 1.9 (4H, m, pyrrolidine), 3.8 (2H, m), 4.1 (1H, m), 6.0 (1H, aromatic), 7.3-8.0 (2H, m), 9.56 (1H, broad, N-H); ms: 188.98 (M^+ , 100%), 160.97 ($M^+ - 28$, 30%), 144.96 ($M^+ - 44$, 92%), 133 (42%).

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.49; H, 5.82; N, 22.22. Found: C, 63.70; H, 5.79; N, 21.91.

4-Aza-7,8,9,10-tetrahydropyrrolo[1,2-*a*]quinoxalin-6-one.

To methyl *N*-(2-nitro-3-pyridyl)piperidine-2-carboxylate (0.5 g, 1.98 mmoles) was added redistilled cyclohexene (2 ml, 25 mmoles) and 10% palladium on charcoal (0.65 g). Absolute ethanol (100 ml) was added before the mixture was heated under reflux for 3 hours. The greenish mixture was filtered through celite after which solvents were completely stripped off leaving a light brown oil, 200 mg (53%); ir: 3300, 1675 (s, lactam C=O), 750 cm^{-1} ; nmr: δ 1.6 (6H, m, piperidine), 4.0 (2H, m), 4.2 (1H, m), 6.0 (1H, aromatic), 7.2-7.4 (2H, m), 9.80 (1H, broad, N-H); ms: 202.96 (M^+ , 100%), 174.96 ($M^+ - 28$, 28%), 158.96 ($M^+ - 44$, 89%), 144

(45%).

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.02; H, 6.40; N, 20.68. Found: C, 64.96; H, 6.08; N, 20.89.

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