Synthesis of Tri- and Tetracyclic Condensed Quinoxalin-2-ones Fused Across the C-3−N-4 Bond

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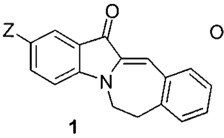
Dedicated to the memory of our dear friend and colleague Dr. Manfred Stud

Keywords: Amino acids / Cyclizations / Nitrogen heterocycles / Rearrangements / Reductions

We have studied the preparation of some fused quinoxalinones by Stevens rearrangement of a spiro-quinoxaline-derived ammonium ylide or by treatment of *N*-(2,4-dinitrophenyl)- and *N*-(2-nitrophenyl)imino acids with different reducing agents. We have reinvestigated and clarified some related processes found in the literature starting from imino acids derivatives. Additional reactions of the fused quinoxalinones, as well as the useful dehydrogenation/decarboxylation of some easily available 1-arylindoline-2-carboxylic acids to the corresponding 1-arylindoles, are also reported.

Introduction

In the last few years we have been developing different methods for the synthesis of betaines and salts derived from indazol-3-ol,[1] indoxyl,[2] cinnolin-3-one,[3] benzothiadiazole 1,1-dioxide,[4] and quinoxalin-2-one,[5] based on intramolecular quaternization reactions. In some cases, the reactive compounds prepared following these procedures were useful intermediates for the preparation of simple and fused indazoles,[6] indoles,[2] and related compounds,[4] some of which have shown a remarkable in vitro activity against HeLa cells.[4]



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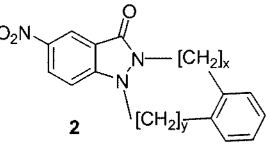
Z = H; NO$_2$



2

x = 1; y = 1
x = 1; y = 2
x = 2; y = 1

Considering the previously studied[2,6] compounds **1** and **2** as models, we decided to prepare some simple and fused quinoxalinones for further testing mainly as cytotoxic agents. Furthermore, many biological properties and technical applications have been reported[7] for compounds containing this heterocyclic system and, in recent years, simple or fused quinoxalinones have become interesting compounds for study in the fields of antihypertensives,[8] vascular smooth muscle relaxants,[8] anti-HIV agents,[9] aldose reductase inhibitors,[10] angiotensin II receptor antagonists,[11] 5-HT$_3$ receptor agonists,[12] and, especially, as GABA/benzodiazepine receptor ligands.[9,13] Owing to the potential biological interest in these compounds, two different solid-phase synthetic methods have been reported recently for the preparation of quinoxalin-2-one libraries.[14]

Results and Discussion

For the preparation of simple and fused quinoxalinones mentioned in the Introduction, we envisaged a synthesis taking advantage of the potential reactivity of some recently reported 3-oxoquinoxalinium salts[5] through a Stevens rearrangement of the corresponding intermediate carbonyl-stabilized ammonium ylides. This method has previously been used[2] to prepare the above-mentioned fused indoles **1**, and the related Wawzonek rearrangement[6] has been used to prepare fused indazoles **2**. In our hands the second process seems to be rather general,[6] but, unfortunately, our present results confirm that the Stevens rearrangement usually takes place only in ylides containing easily migrating groups linked to the quaternary nitrogen atom.[2,15,16] Thus, starting from a series of the previously mentioned quinoxalinium salts,[5] we could only prepare quinoxalinone **5**, arising from 1,2,3,4-tetrahydroisoquinoline-derived compound **3**, through the rearrangement of the "benzyl moiety" of the intermediate ylide **4** (Scheme 1). Attempts to prepare other fused quinoxalinones, e.g., compound **48** (see below) from the pyrrolidine analogue[5] of salt **3**, gave only complex

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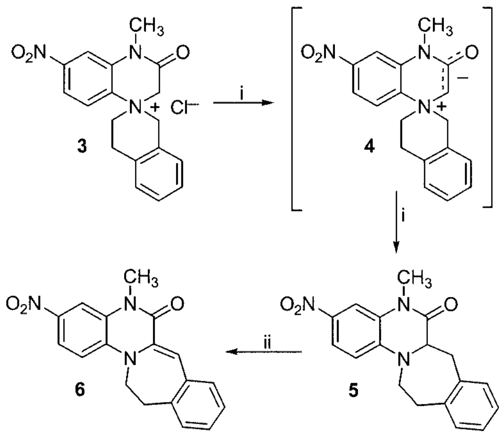
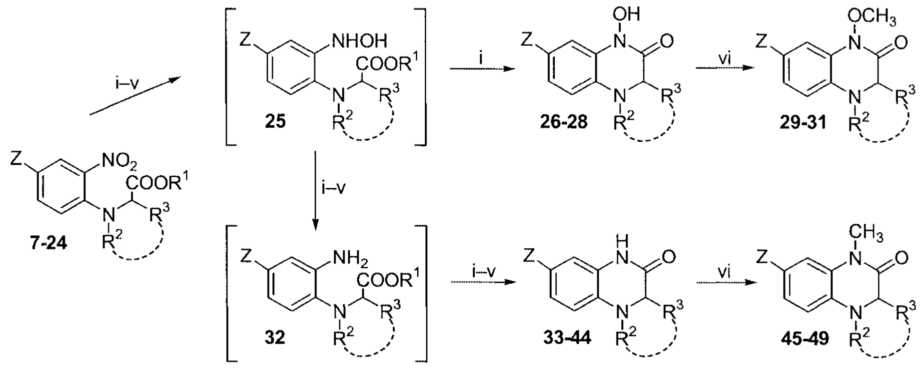


Scheme 1. Reagents and conditions: (i) aq. NaOH, room temperature; (ii) MnO_2, $CHCl_3$, room temperature

mixtures that probably are produced via the corresponding carbenes,[15] without traces of the desired compounds.

To develop a general procedure for the preparation of the desired quinoxalinones, we outlined an alternative synthesis (Scheme 2) starting from *N*-(2,4-dinitrophenyl)- (DNP-) (**7**−**12**) or *N*-(2-nitrophenyl)- (NP-) (**15**−**20**) derivatives of *N*-alkylamino acids and cyclic imino acids. These compounds are readily available from the corresponding imino acids and, respectively, 1-fluoro-2,4-dinitrobenzene[17] or 1-fluoro-2-nitrobenzene.[18,19] Indole-2-carboxylic acid does not react under the conditions used for other imino acids and it seems that the copper-catalyzed *N*-arylation (Ullmann reaction) of this compound does not proceed well with 1-halo-2-nitroarenes.[20] Additional attempts[21] to prepare the DNP- and NP derivatives of indole-2-carboxylic acid by dehydrogenation of indoline analogues **11** and **19** with manganese(IV) oxide[22a] gave 1-arylindoles **50** and **51** through an unexpected concomitant decarboxylation. Decarboxylation of indole-2-carboxylic acid derivatives is a well-known process, but it usually requires special conditions, such as high temperatures or the use of copper derivatives or bases as catalysts.[22b]

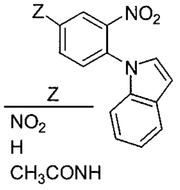
In the case of nitroquinoxalinones **33**−**38**, we expected that DNP derivatives **7**−**12**, through a selective reduction of the 2′-NO_2 group to an NH_2 group followed by spontaneous lactamization of the intermediates **32**, could afford the desired products (Scheme 2). Starting from DNP derivatives of the usual α-amino acids, ammonium[23,24] or sodium[24,25] sulfides and sodium hydrosulfide[26] (Zinin reaction),[27] as well as tin(II) chloride,[23,24] have been used with these targets in mind, but, according to the extensive study of Scoffone et al.,[24] ammonium sulfide seems to be the preferred reagent. In our hands, this method proceeds effectively as reported with DNP-glycine, but when applied



Z = NO_2	Z = H	R^2, R^3
7 (R^1 = H), **26**, **29**, **33**, **45**	**15** (R^1 = H), **21** (R^1 = CH_3), **39**	CH_3, H
8 (R^1 = H), **13** (R^1 = CH_3), **27**, **30**, **34**, **46** (*)	**16** (R^1 = H), **22** (R^1 = CH_3), **40** (*)	$[CH_2]_3$
9 (R^1 = H), **35**, **47**	**17** (R^1 = H), **23** (R^1 = CH_3), **41**	$[CH_2]_3$
10 (R^1 = H), **14** (R^1 = CH_3), **28**, **31**, **36**, **48**	**18** (R^1 = H), **24** (R^1 = CH_3), **42**	$[CH_2]_4$
11 (R^1 = H), **37**	**19** (R^1 = H), **43**	*o*-$C_6H_4CH_2$
12 (R^1 = H), **38**, **49**	**20** (R^1 = H), **44**	*o*-$CH_2C_6H_4CH_2$

(*): (*S*)-compounds

Scheme 2. Reagents and conditions: (i) from **7**, **8**, and **10**, (a) $(NH_4)_2S$, $EtOH/H_2O$, 45−50 °C, (b) aq. HCl (pH 1), 70 °C; (ii) from **7**−**12**, (a) $NaHCO_3$, Na_2S, $MeOH/H_2O$, room temperature, (b) AcOH (pH 4); (iii) from **15**−**18** and **21**−**24**, H_2 (20 psi), 10% Pd/C, EtOH, 30 °C; (iv) from **22**, cyclohexene, 5% Pd/C, EtOH, reflux (from **13** and **14**, see Schemes 3 and 4); (v) from **15**−**20**, K_2CO_3, $Na_2S_2O_4$, H_2O, room temperature; (vi) MeI, K_2CO_3, acetone, 80−90 °C (autoclave)



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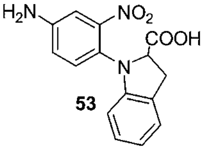
51
52



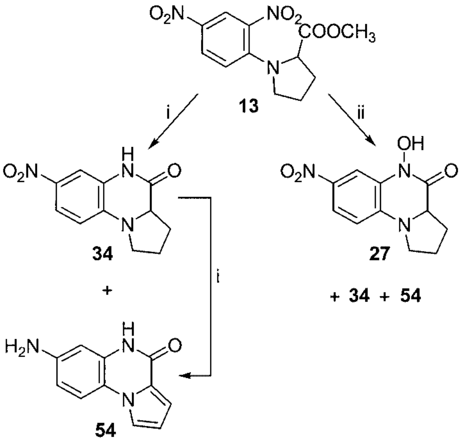
53

to derivatives of *N*-alkylamino acids or cyclic imino acids, such as DNP-sarcosine (**7**), DNP-L-proline (**8**), and DNP-DL-pipecolic acid (**10**), it gave mixtures of the desired quinoxalin-2-ones[28] (**33**, **34**, and **36**) together with the corresponding 1-hydroxy derivatives (**26**−**28**) arising from the cyclization of hydroxylamino derivatives **25**, postulated[27] as intermediates in the Zinin reduction of nitro compounds to the respective amines (Scheme 2). The mixtures (**26**/**33**, ca. 75:25 molar ratio; **27**/**34** and **28**/**36**, ca. 60:40 molar ratio as determined by ^1H NMRspectroscopy) were separated by column chromatography, but 1-hydroxyquinoxalin-2-ones **26**−**28** were rather unstable and, for characterization, they were immediately converted into the corresponding 1-methoxy derivatives **29**−**31** by treatment with methyl iodide. Alternatively, methylation of the crude mixtures of quinoxalinones **33**, **34**, and **36** and the corresponding 1-hydroxy derivatives **26**−**28** afforded mixtures of 1-methyl- (**45**, **46**, **48**) and 1-methoxyquinoxalinones (**29**−**31**), which were also separated by chromatography. 1-Methylquinoxalinones **45**−**49** were also prepared by methylation of isolated quinoxalinones **33**−**36** and **38**.

On the other hand, treatment of DNP derivatives **7**−**12** with sodium sulfide, following the method used by Berg and Parnell[25] to cyclize DNP-glycine with some modifications, afforded, in most cases, the desired quinoxalinones **33**−**38** containing only traces of the corresponding 1-hydroxy derivatives, which were easily removed by chromatography. As an exception, the DNP derivative of indoline-2-carboxylic acid (**11**) afforded the desired tetracyclic quinoxalinone **37** in very low yield together with compound **53** arising from the reduction of the 4′-NO_2 group of the starting material. We have not found an explanation for this reversal of selectivity that is found in the remaining DNP-amino and -imino acids. Attempts to purify compound **53** led to extensive decomposition and for this reason it could only be partially characterized, and its structure was deduced initially from analysis of its ^1H NMR and mass spectra. Nevertheless, compound **53**, after acetylation of the amino group and treatment with manganese(IV) oxide afforded, through the previously mentioned dehydrogenation/decarboxylation of the indoline-2-carboxylic acid moiety, the fully characterized 1-arylindole **52**. The NOE observed between the NH proton and 3′- and 5′-H of this compound was essential to establish its structure and, consequently, to deduce that of compound **53**.

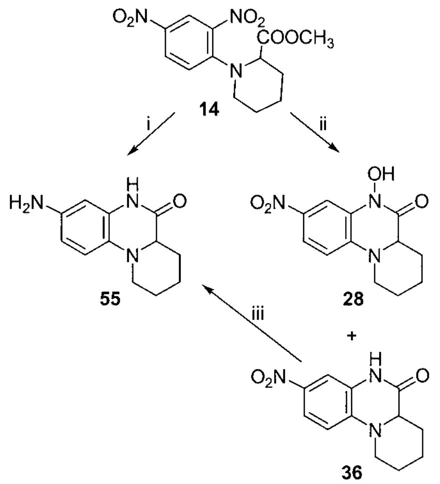
The preparation of fused quinoxalinones **34** and **36** by treatment of methyl esters of DNP-L-proline (**13**) and DNP-DL-pipecolic acid (**14**) with cyclohexene−Pd/C in ethanol has been claimed by Alo and co-workers.[29,30] The ^1H NMR spectra and some of the reported physical properties (m.p., solubility, etc.) of the compounds prepared by these authors, however, are completely different from those found by us in our quinoxalinones. To clarify these discrepancies, we decided to repeat Alo and co-workers' experimental procedures and found that they are not convenient methods for the preparation of quinoxalinones **34** and **36** because they yield other products or mixtures that cannot be separated following the described purification methods.

Thus, starting from DNP-L-proline methyl ester **13** and using 10% Pd/C, following exactly the procedure of Alo and co-workers,[29] we obtained a mixture (molar ratios in ^1H NMR spectra) of **34** (11%) and the dehydrogenated amino derivative **54** (89%) (Scheme 3). In separate experiments we found that compound **54** was produced from **34** (or **35**) under Alo's experimental conditions. On the other hand, using 5% Pd/C (conditions only assayed by the mentioned group[30] starting from ester **14**), we obtained a mixture of 1-hydroxy derivative[28] **27** (23%), quinoxalinone **34** (61%), starting ester **13** (10%), and amine **54** (6%).



Scheme 3. Reagents and conditions: (i) cyclohexene, 10% Pd/C, EtOH, reflux; (ii) cyclohexene, 5% Pd/C, EtOH, reflux

In the case of DNP-DL-pipecolic acid methyl ester **14**, Alo and co-workers have reported its reduction/cyclization using cyclohexene and both 10 and 5% Pd/C. In the first case,[29] they obtained "anhydrous **36**" (m.p. 290 °C) while in the second,[30] a compound claimed to be "**36** monohydrate" (m.p. 188−190 °C) was isolated. In our hands, however, the procedure using 10% Pd/C yielded aminoquinoxalinone **55** that is identical to the compound we prepared by catalytic hydrogenation of authentic nitroquinoxalinone **36** (Scheme 4). The preparation of aminoquinoxalinone **55** by reduction of their "nitroquinoxalinone **36**" with tin/hydrochloric acid has been claimed[18] by Adegoke and Alo, but, again, the m.p. and ^1H NMR spectrum of the product obtained by these authors are not in agreement with those found by us. Starting also from ester **14**, but using 5% Pd/C, we obtained a mixture (molar ratios in ^1H NMR spectrum) of authentic nitroquinoxalinone **36** (5%), the corresponding 1-hydroxy derivative[28] **28** (87%) and starting ester **14** (8%) (Scheme 4).



Scheme 4. Reagents and conditions: (i) cyclohexene, 10% Pd/C, EtOH, reflux; (ii) cyclohexene, 5% Pd/C, EtOH, reflux; (iii) H_2 (15 psi), 10% Pd/C, pyridine, room temperature

On the other hand, quinoxalinones **39−44** (Scheme 2), which lack a NO_2 group in the benzene ring, were prepared starting from NP derivatives of imino acids, such as **15−20**. Several methods have been reported — e.g., catalytic hydrogenation (hydrogen−Pd/C),[13a] hydrogen transfer (cyclohexene−Pd/C,[18,30] formic acid−Pd/C and ammonium formate−Pd[31]), treatment with sodium dithionite,[8,30] iron/acetic acid,[8,31] tin(II) chloride,[14] tin/hydrochloric acid[32] — for the reduction/cyclization of compounds of this kind and related derivatives, including the corresponding esters **21−24**.

To compare some of these methods, acids **15−20** were cyclized to the respective quinoxalinones **39−44** by catalytic hydrogenation and/or by treatment with sodium dithionite; methyl esters **21−24**, in turn, have been cyclized by catalytic hydrogenation and, additionally for ester **22**, also by hydrogen transfer (cyclohexene−Pd/C). Yields are similar in all cases, but the cyclization with sodium dithionite seems to be the preferred method: it starts from the acids, the obtained crude quinoxalinones are very pure, and the experimental procedure is very simple and fast. Furthermore, when applied to L-proline derivative **16**, the reaction proceeds always without racemization of imino acid moiety (see below).

Adegoke and Alo[18] claimed the preparation of pyrrolo[1,2-*a*]quinoxalinone **40** following two different methods: a) by reduction of their "7-nitro analogue **34**" (see above) to the corresponding amine, followed by deamination through the diazonium salt, and b) by reduction/cyclization of NP-L-proline methyl ester **22** by means of cyclohexene−Pd/C. In both cases, starting from L-proline, the m.p. of the obtained compound (174−175 °C) is rather different from that obtained by us (m.p. 163−165 °C) and practically identical to that of the corresponding racemic derivative **41** (m.p. 174.5−176 °C) prepared[33] from racemic ethyl 2-bromo-5-chlorovalerate and *o*-phenylenediamine through two consecutive cyclization reactions.

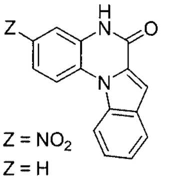
Furthermore, rather different values of the m.p. have been recorded by the same research group for pyrido[1,2-*a*]quinoxalinone **42**. Thus, m.p. 148−149 °C was recorded[18] for this compound when prepared following the procedures mentioned above for compound **40**, but, in a following paper,[30] m.p. 189−190 and 190−191 °C (practically identical to that we found: m.p. 192−194 °C) were given for compound **42** prepared by reduction/cyclization of NP-DL-pipecolic acid **18** with sodium dithionite and from its methyl ester **24** by treatment with cyclohexene−Pd/C, respectively.

The eventual racemization of amino or imino acid moieties is an aspect of these processes that has not thoroughly been studied in the literature. In fact, this problem has only been treated in the above-mentioned papers dealing with the solid-phase synthesis of quinoxalinones. Lee and coworkers[14a] suggested that the racemization observed in some final products could originate during *N*-arylation of the amino acids, but Morales et al.[14b] found that racemization of amino acid moieties occurs in the cleavage of the final quinoxalinone from the resin upon treatment with trifluoroacetic acid.

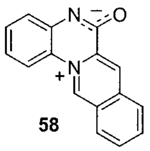
We have carried out some experiments with the optically active NMR spectroscopic shift reagent (+)-Eu(hfc)$_3$, in which we compared the behavior of our L-proline, DL-proline, and DL-pipecolic acid derivatives. Thus, it was possible to deduce that no noticeable racemization of the L-proline moiety occurs in either a) *N*-arylation of L-proline with 1-fluoro-2,4-dinitro- or 1-fluoro-2-nitrobenzene to give compounds **8** and **16**, b) the esterification of the latter to the corresponding methyl esters **13** and **22**, c) the cyclization of compound **8** to quinoxalinones **27** and/or **34** by treatment with ammonium or sodium sulfides and that of compound **16** to quinoxalinone **40** with sodium dithionite, or d) methylation of quinoxalinones **27** and **34** to the corresponding *N*-methoxy (**30**) and *N*-methyl (**46**) derivatives. On the other hand, catalytic hydrogenation of L-proline-derived acid **16** or its methyl ester **22** to afford **40** proceeds sometimes with slight racemization [≥ 90% *ee* in a series of experiments (e.r. ≥ 95:5)] and cyclization of esters **13** and **22** by hydrogen transfer (cyclohexene, 5% Pd/C) yields enantiomerically pure compound **34** and partially racemized compound **40** [50−70% *ee* in a series of experiments (e.r. = 75:25−85:15)] respectively. We did not study the enantiomeric composition of quinoxalinone **34** arising from the cyclization of ester **13** using 10% Pd/C.

We suppose that racemization of compound **40**, in processes that use Pd/C as the catalyst, can take place through an equilibrium in which the corresponding 3,3a-dehydro derivative is involved. In fact, one of these partially dehydrogenated compounds may be postulated as an intermediate in the transformation of pyrrolidine derivative **34** into the fused pyrrole **54** (Scheme 3). Nevertheless, the study of other amino acid-derived quinoxalinones is required to explain how NO_2 group prevents racemization of compound

34 and to ascertain if racemization observed for **40** is specific for proline derivatives or otherwise.



56 Z = NO_2
57 Z = H



58

Finally, dehydro derivatives **6** (Scheme 1), **56** and **57** were obtained, respectively, by treatment of quinoxalinones **5**, **37**, and **43** with iron(III) chloride and/or manganese(IV) oxide; quinoxalinone **44**, when treated with the iron salt, afforded a strongly polar compound for which the betaine structure **58** has been deduced.

Conclusion

We have studied two different approaches directed at the preparation of polycyclic quinoxalin-2-ones[28] fused across the C-3−N-4 bond. The first procedure, based on the Stevens rearrangement of quinoxaline-derived ammonium ylides, is affected by the peculiar limitations of this process and, in fact, it seems that it can be applied only to substrates containing easily migrating groups. Nevertheless, the fused quinoxalinones could be readily prepared following an alternative method based on the reduction of the 2′-NO_2 group of *N*-(2,4-dinitrophenyl)- or *N*-(2-nitrophenyl)imino acids followed by lactamization; a careful selection of the reagents needed for the reduction of the NO_2 group is required, however, to achieve pure final products and to preserve the eventual chirality of the imino acid moieties involved.

Experimental Section

General Remarks: Melting points were determined in a Reichert−Jung Thermovar hot-stage microscope equipped with a polarizer. Optical rotations were measured with a Perkin−Elmer 241 MC polarimeter in a 1-dm cell. IR spectra were obtained on a Perkin−Elmer Spectrum One spectrophotometer. ^1H (300 or 400 MHz) and ^{13}C (75 or 100 MHz) NMR spectra were recorded on Varian Unity 300 or Varian Inova 400 spectrometers. The chemical shifts are reported in ppm from TMS (δ scale), but were usually measured against the solvent signal; 1,4-dioxane was used as reference for the ^{13}C NMR spectrum of betaine **58** in D_2O. The assignments were made by means of different standard homonuclear and heteronuclear correlation experiments (NOE, COSY, HMQC, and HMBC). Electron impact (EI) and electrospray (ES) mass spectra were obtained, respectively, at 70 eV on a Hewlett Packard 5973 MSD and on a Hewlett Packard 1100 MSD spectrometer. DC-Alufolien silica gel 60 PF_{254} (Merck, layer thickness 0.2 mm) was used for TLC. Flash column chromatography was carried out on silica gel 60 (Merck, particle size 0.040−0.063 mm). Microanalyses were performed by the Departamento de Análisis, Centro de Química Orgánica "Manuel Lora Tamayo", CSIC, Madrid, Spain.

Stevens Rearrangement of Quinoxalinium Ylide 4. Preparation of Fused Quinoxalinone 5: A solution of sodium hydroxide (0.16 g, 4.0 mmol) in water (10 mL) was added to a solution of quinoxalinium chloride **3**[5] (0.36 g, 1.0 mmol) in water (20 mL). The mixture was stirred for 30 min and then the suspended yellow solid was extracted with chloroform (3 × 20 mL). The solution was dried with magnesium sulfate and the solvent evaporated to afford practically pure (^1H NMR) quinoxalinone **5**.

5-Methyl-3-nitro-6a,7,12,13-tetrahydro-5*H*-[3]benzazepino[3,2-*a*]-quinoxalin-6-one (5): Yield: 0.31 g (96%); m.p. 187−189 °C (1-propanol). IR (KBr): $\tilde{\nu}$ = 1681 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.02 (dd, *J* = 9.1, 2.4 Hz, 1 H, 2-H), 7.85 (d, *J* = 2.4 Hz, 1 H, 4-H), 7.16 (m, 4 H, 8-, 9-, 10-, 11-H), 6.78 (d, *J* = 9.1 Hz, 1 H, 1-H), 4.27 (d, *J* = 10.0 Hz, 1 H, 6a-H), 4.18 (dd, *J* = (−)14.6, 5.1 Hz, 1 H, 13-H_A), 3.47 (s, 3 H, CH_3), 3.41 (dd, *J* = (−)14.9, 11.5 Hz, 1 H, 12-H_A), 3.29 (dd, *J* = (−)14.6, 11.5 Hz, 1 H, 13-H_B), 3.17 (dd, *J* = (−)14.8, 10.0 Hz, 1 H, 7-H_A), 2.89 (d, *J* = (−)14.8 Hz, 1 H, 7-H_B), 2.83 (dd, *J* = (−)14.9, 5.1 Hz, 1 H, 12-H_B) ppm. ^{13}C NMR ($CDCl_3$): δ = 165.4 (C-6), 139.9, 139.4, 139.1, 138.3 (C-3, -7a, -11a, -14a), 128.4 (C-4a), 130.5, 129.9, 127.3, 127.1 (C-8, -9, -10, -11), 121.2 (C-2), 111.5 (C-1), 110.6 (C-4), 63.8 (C-6a), 48.6 (C-13), 40.1 (C-7), 34.2 (C-12), 29.3 (CH_3) ppm. EI MS: *m/z* (%) = 323 (52) [M^+], 308 (3), 294 (7), 204 (6), 190 (4), 178 (4), 144 (6), 131 (10), 130 (10), 117 (100), 105 (15), 91 (26). $C_{18}H_{17}N_3O_3$ (323.35): calcd. C 66.86, H 5.30, N 13.00; found C 66.84, H 5.18, N 12.82.

Preparation of *N*-(2,4-Dinitrophenyl)imino Acids (7−12): These compounds were prepared from the corresponding *N*-alkylamino or cyclic imino acids [sarcosine, L- and DL-proline, DL-pipecolic acid, indoline-2-carboxylic acid, or 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride (18 mmol)], 1-fluoro-2,4-dinitrobenzene (3.72 g, 20 mmol) and sodium hydrogencarbonate (3.78 g, 45 mmol for compounds **7**−**11**; 5.04 g, 60 mmol for compound **12**) in ethanol/water (1:1, 200 mL), following the procedure of Rao and Sober.[17] After acidification, the precipitated solids (or gums that solidified) were isolated by filtration. The crude compounds were practically pure (TLC, ^1H NMR) and were used directly in further steps. DNP-sarcosine (**7**): 96% yield, m.p. 174−176 °C (methanol), ref.[26] 176 °C, ref.[34] 170−172 °C; DNP-L-proline (**8**): 92% yield, m.p. 136−138 °C (benzene), ref.[17] 138 °C; DNP-DL-proline (**9**): 96% yield, m.p. 179−180 °C (methanol), ref.[17] 181 °C; DNP-DL-pipecolic acid (**10**): 91% yield, m.p. 131−132 °C (toluene), ref.[17] 138−139 °C, ref.[29] 130−131 °C.

1-(2,4-Dinitrophenyl)indoline-2-carboxylic Acid (11): Yield: 5.57 g (94%). Attempts to recrystallize this compound resulted in extensive decomposition. An analytical sample was prepared by dissolution of the product in aq. sodium hydrogen carbonate followed by treatment with charcoal, filtration and reprecipitation with aq. hydrochloric acid; m.p. 116−118 °C (decomp.). IR (nujol): $\tilde{\nu}$ = 1723 (CO) cm^{-1}. ^1H NMR ([D_6]DMSO): δ = 8.76 (d, *J* = 3.1 Hz, 1 H, 3′-H), 8.46 (dd, *J* = 9.0, 3.1 Hz, 1 H, 5′-H), 7.59 (d, *J* = 9.0 Hz, 1 H, 6′-H), 7.28 (d, *J* = 7.5 Hz, 1 H, 4-H), 7.07 (dd, *J* = 7.5, 7.5 Hz, 1 H, 6-H), 6.93 (dd, *J* = 7.5, 7.5 Hz, 1 H, 5-H), 6.52 (d, *J* = 7.5 Hz, 1 H, 7-H), 5.25 (dd, *J* = 10.0, 5.1 Hz, 1 H, 2-H), 3.63 (dd, *J* = (−)15.9, 10.0 Hz, 1 H, 3-H_A), 3.27 (dd, *J* = (−)15.9, 5.1 Hz, 1 H, 3-H_B) ppm. ^{13}C NMR ([D_6]DMSO): δ = 172.2 (CO), 143.9 (C-7a), 141.1, 140.0, 138.6 (C-1′, -2′, -4′), 130.1 (C-3a), 128.7 (C-5′), 127.1 (C-6), 125.5 (C-4), 123.8 (C-6′), 123.2 (C-3′), 122.7 (C-5), 109.0 (C-7), 66.0 (C-2), 33.8 (C-3) ppm. EI MS: *m/z* (%) = 329 (27) [M^+], 284 (48), 250 (33), 239 (36), 206 (29), 191 (100), 179

(33), 163 (27), 89 (21). $C_{15}H_{11}N_3O_6$ (329.3): calcd. C 54.72, H 3.37, N 12.76; found C 54.99, H 3.21, N 12.60.

2-(2,4-Dinitrophenyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (12): Yield: 6.00 g (97%); m.p. 181−182 °C (decomp., ethanol). IR (nujol): $\tilde{\nu}$ = 1718 (CO) cm^{-1}. ^1H NMR ([D_6]DMSO): δ = 8.69 (d, *J* = 2.9 Hz, 1 H, 3′-H), 8.36 (dd, *J* = 9.5, 2.9 Hz, 1 H, 5′-H), 7.52 (d, *J* = 9.5 Hz, 1 H, 6′-H), 7.20 (m, 4 H, 5-, 6-, 7-, 8-H), 4.66 (dd, *J* = 5.4, 3.2 Hz, 1 H, 3-H), 4.61 (d, *J* = (−)16.1 Hz, 1 H, 1-H_A), 4.31 (d, *J* = (−)16.1 Hz, 1 H, 1-H_B), 3.34 (dd, *J* = (−)16.1, 5.4 Hz, 1 H, 4-H_A), 3.24 (dd, *J* = (−)16.1, 3.2 Hz, 1 H, 4-H_B) ppm. ^{13}C NMR ([D_6]DMSO): δ = 171.4 (CO), 149.1 (C-1′), 137.7, 137.1 (C-2′, -4′), 132.1 (two superimposed signals, C-4a, -8a), 128.2 (C-5′), 128.5, 126.9, 126.5, 126.3 (C-5, -6, -7, -8), 123.5 (C-3′), 120.3 (C-6′), 59.2 (C-3), 49.3 (C-1), 30.1 (C-4) ppm. EI MS: *m*/*z* (%) = 343 (0.5) [M^+], 342 (1), 326 (33), 309 (14), 298 (49), 281 (40), 264 (66), 249 (26), 218 (72), 205 (100), 190 (17), 178 (12), 164 (17), 130 (26), 115 (45), 103 (64), 91 (51). $C_{16}H_{13}N_3O_6$ (343.3): calcd. C 55.98, H 3.82, N 12.24; found C 56.21, H 4.08, N 12.53.

Reduction/Cyclization of *N*-(2,4-Dinitrophenyl) Compounds to Quinoxalinone Derivatives

Method a. Treatment of *N*-(2,4-Dinitrophenyl)imino Acids 7, 8, and 10 with Ammonium Sulfide: Ammonium sulfide solution (20 mL; prepared by saturation of 15% aq. ammonium hydroxide with hydrogen sulfide) was added to a suspension of the corresponding DNP-imino acid (**7**, **8**, **10**; 10 mmol) in ethanol (20 mL). The solution was heated at 45−50 °C for 30 min, acidified at pH 1 with 6 M aq. hydrochloric acid, and heated at 70 °C for 15 min. After cooling, the precipitate was collected by filtration, washed with water, and air-dried. To separate the sulfur, the solid thus obtained was triturated and heated under reflux for 10 min with carbon tetrachloride (50 mL), recovered by filtration and washed with the same solvent (3 × 10 mL). The solids obtained were shown to be (^1H NMR) mixtures of quinoxalinones **33**, **34**, and **36** and the corresponding *N*-hydroxy derivatives **26**, **27**, and **28** (**26**/**33**, 75:25 molar ratio, 1.65 g; **27**/**34**, 60:40 molar ratio, 1.52 g; **28**/**36**, 60:40 molar ratio, 1.80 g). The mixtures were then treated according to one of these methods:

a_1) In each case, the mixture (0.5 g) was triturated with silica gel and applied to the top of a silica gel chromatography column. Quinoxalinones **33**, **34**, and **36** were eluted with chloroform/acetone (20:1 to 10:1) mixtures and *N*-hydroxy derivatives **26**, **27**, and **28** using chloroform/methanol (30:1 to 10:1) mixtures; in both cases the compounds were obtained by evaporation to dryness of the respective fractions. Owing to their low stability, compounds **26**−**28** were immediately methylated as described below for quinoxalinones **33**−**36**, and **38**, affording *N*-methoxy derivatives **29**−**31**.

a_2) In each case, the crude product (0.5 g) was methylated as described below for quinoxalinones **33**−**36**, and **38**. The respective mixtures of *N*-methyl- (**45**, **46**, **48**) and *N*-methoxyquinoxalinones (**29**−**31**) were separated, following this elution order, by column chromatography using hexane/ethyl acetate (10:1 to 2:1) mixtures.

Method b. Treatment of *N*-(2,4-Dinitrophenyl)imino Acids 7−12 with Sodium Sulfide: A solution of sodium hydrogen carbonate (2.52 g, 30 mmol) in water (30 mL) was added to a suspension of the corresponding DNP-imino acid (**7**−**12**; 10 mmol) in methanol (30 mL). A solution of sodium hydrogen carbonate (2.52 g, 30 mmol) and sodium sulfide nonahydrate (7.69 g, 32 mmol) in water (30 mL) was added to the resulting solution. The mixture was stirred at 30 °C for 1−4 h until consumption of most of the starting material and then acidified (pH 4) with acetic acid. The precipitated solid was collected by filtration, washed with water, air-dried, and treated with refluxing carbon tetrachloride as described in Method A to remove sulfur. To separate traces of *N*-hydroxyquinoxalinones (**26**−**28** and analogues) and some tars, the solids obtained were triturated with silica gel and applied to the top of a short silica gel chromatography column from which quinoxalinones **33**−**38** were eluted with chloroform/methanol (40:1 to 10:1) mixtures.

Method c. Treatment of *N*-(2,4-Dinitrophenyl)imino Acid Methyl Esters 13 and 14 with Cyclohexene−Pd/C: The required methyl esters **13** and **14** were prepared by sulfuric acid-catalyzed esterification of DNP-L-proline (**8**) and DNP-DL-pipecolic acid (**10**), respectively.[29,30]

c_1) Reaction with 10% Pd/C: The method of Alo and co-workers[29] was followed initially in both cases, but some modifications were introduced to isolate the resulting products. Starting from L-proline derivative **13**, a mixture of this ester (1.50 g, 5.1 mmol), redistilled cyclohexene [3.20 g, 4 mL, 39.4 mmol ("4 mL, 50 mmol" according to the authors)] and 10% Pd/C (5 g) in ethanol (50 mL) was heated under reflux for 2 h. After cooling, the mixture was filtered through Celite and the cake washed with ethanol (3 × 25 mL) and pyridine (3 × 25 mL). The combined solution was evaporated to dryness affording a solid that contained, together with some unidentified by-products and tars with low values of R_f (TLC), an 11:89 mixture (^1H NMR, molar ratio) of derivatives **34** and **54**. These compounds were isolated, in the order indicated, by chromatography on a silica gel column using chloroform/methanol (75:1 to 20:1) mixtures as eluent.

Starting from pipecolic acid derivative **14**, a mixture of this ester (1.00 g, 3.2 mmol) and the above-mentioned amounts of cyclohexene, 10% Pd/C, and ethanol was heated under reflux for 2 h. The catalyst was filtered off and the filtrate evaporated to dryness to afford a residue that was shown to be (^1H NMR) aminoquinoxalinone **55**.

c_2) Reaction with 5% Pd/C: The method reported by Alo and co-workers[30] for the reduction/cyclization of ester **14** was followed exactly in both cases. A mixture of each ester (1.50 g; 5.1 mmol of compound **13** and 4.85 mmol of compound **14**), redistilled cyclohexene (2.6 mL) and 5% Pd/C (0.80 g) in ethanol (32 mL) was heated under reflux for 2 h. After cooling, the mixtures were filtered through Celite, the cake washed as in method c_1 and the solvent was evaporated to dryness. Starting from ester **13**, the solid obtained (1.03 g) was analyzed by ^1H NMR spectroscopy, which indicated that it contained a mixture (molar ratios) of *N*-hydroxy derivative **27** (23%), quinoxalinone **34** (61%), starting material **13** (10%) and amino derivative **54** (6%); quinoxalinone **34** was isolated by column chromatography as indicated in method c_1. In the case of ester **14**, the solid obtained (1.21 g) contained a mixture of *N*-hydroxy derivative **28** (87%), quinoxalinone **36** (5%) and starting material **14** (8%); no attempts were made to separate this mixture.

***N*-Hydroxyquinoxalinones 26−28:** These compounds were prepared from DNP-imino acids **7**, **8**, and **10** following Method a_1 and, after chromatographic separation, they were immediately methylated to the corresponding *N*-methoxy derivatives **29**−**31**. ^1H NMR spectroscopic data of *N*-hydroxyquinoxalinones are given mainly to allow their identification in the crude mixtures obtained following Methods a, b, and c_2.

1-Hydroxy-4-methyl-7-nitro-3,4-dihydro-1*H*-quinoxalin-2-one (26): ^1H NMR ([D_6]DMSO): δ = 10.97 (br. s, 1 H, OH), 7.87 (m, 2 H, 6-, 8-H), 6.75 (d, J = 9.1 Hz, 1 H, 5-H), 4.21 (s, 2 H, 3-H), 2.93 (s, 3 H, CH_3) ppm.

(*S*)-5-Hydroxy-7-nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (27): ^{1}H NMR ([D$_6$]DMSO): δ = 10.92 (br. s, 1 H, OH), 7.90 (dd, J = 8.8, 2.6 Hz, 1 H, 8-H), 7.82 (d, J = 2.6 Hz, 1 H, 6-H), 6.65 (d, J = 8.8 Hz, 1 H, 9-H), 4.33 (m, 1 H, 3a-H), 3.45 (m, 2 H, 1-H), 2.26 (m, 1 H, 3-H$_A$), 2.00 (m, 3 H, 2-H, 3-H$_B$) ppm. EI MS: m/z (%) = 249 (50) [M$^+$], 232 (91), 204 (84), 186 (62), 177 (61), 158 (100), 130 (27), 118 (12), 117 (12), 103 (15), 89 (13).

5-Hydroxy-3-nitro-7,8,9,10-tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (28): ^{1}H NMR ([D$_6$]DMSO): δ = 11.01 (br. s, 1 H, OH), 7.88 (m, 2 H, 2-, 4-H), 7.00 (d, J = 9.0 Hz, 1 H, 1-H), 4.16 (m, 1 H, 6a-H), 3.98 (br. d, J = (−)13 Hz, 1 H, 10-H$_A$), 2.94 (br. dd, J = (−)13, 13 Hz, 1 H, 10-H$_B$), 2.10−1.40 (m, 6 H, 7-, 8-, 9-H) ppm. EI MS: m/z (%) = 263 (33) [M$^+$], 246 (100), 218 (77), 200 (42), 190 (14), 172 (67), 163 (28), 144 (14), 133 (13), 117 (20), 105 (15), 97 (12), 90 (13).

Quinoxalinones 33−38: These compounds were prepared from DNP-imino acids **7**−**12** following Methods a$_1$ and/or b and, in the case of quinoxalinone **34**, also from DNP-L-proline methyl ester **13** following Methods c$_1$ and c$_2$.

4-Methyl-7-nitro-3,4-dihydro-1*H*-quinoxalin-2-one (33): Yield: 63 mg (10%) (Method a$_1$), 1.35 g (65%) (Method b); m.p. 262−264 °C (decomp., pyridine/water), ref.[5] m.p. 262−264 °C.

(*S*)-7-Nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (34): Yield: 184 mg (24%) (Method a$_1$), 1.45 g (62%) (Method b), 95 mg (8%) (Method c$_1$), 0.63 g (53%) (Method c$_2$); m.p. 252−254 °C (decomp., pyridine/water); a product claimed to be quinoxalinone **34** has been described,[29] but the reported m.p. (288 °C) as well as the spectroscopic data are completely different from those found by us. $[\alpha]_D^{22}$ = −646.8 (c = 0.1, pyridine). IR (KBr): $\tilde{\nu}$ = 1677 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.71 (br. s, 1 H, NH), 7.82 (dd, J = 8.9, 2.6 Hz, 1 H, 8-H), 7.62 (d, J = 2.6 Hz, 1 H, 6-H), 6.61 (d, J = 8.9 Hz, 1 H, 9-H), 4.07 (dd, J = 9.5, 6.3 Hz, 1 H, 3a-H), 3.46 (m, 2 H, 1-H), 2.22 (m, 1 H, 3-H$_A$), 1.97 (m, 3 H, 2-H, 3-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 165.4 (C-4), 140.0 (C-9a), 136.8 (C-7), 126.5 (C-5a), 120.5 (C-8), 109.8 (C-9), 109.2 (C-6), 59.0 (C-3a), 46.5 (C-1), 27.5 (C-3), 21.7 (C-2) ppm. EI MS: m/z (%) = 233 (61) [M$^+$], 204 (31), 186 (10), 177 (100), 158 (10), 131 (31), 117 (7), 104 (7), 90 (8). $C_{11}H_{11}N_3O_3$ (233.2): calcd. C 56.65, H 4.75, N 18.02; found C 56.80, H 5.04, N 18.31.

7-Nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (35): Yield: 1.47 g (63%) (Method b); m.p. 256−259 °C (decomp., pyridine/water). IR (KBr): $\tilde{\nu}$ = 1679 (CO) cm^{-1}. Other spectroscopic data are identical to those of *S* enantiomer **34**. $C_{11}H_{11}N_3O_3$ (233.2): calcd. C 56.65, H 4.75, N 18.02; found C 56.85, H 5.01, N 17.96.

3-Nitro-7,8,9,10-tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (36): Yield: 180 mg (26%) (Method a$_1$), 1.61 g (65%) (Method b); crystals (pyridine/water) of compound **36** decompose with darkening from ca. 225 °C and they lose their birefringence (polarized light, crossed nicols) at 270−280 °C, but a clear m.p. is not observed. A product claimed to be quinoxalinone **36** has been described, but the reported m.p.s (290 °C,[29] 188−190 °C[30]) as well as the spectroscopic data[29] are completely different from those found by us. IR (KBr): $\tilde{\nu}$ = 1676 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.78 (br. s, 1 H, NH), 7.80 (dd, J = 9.2, 2.7 Hz, 1 H, 2-H), 7.62 (d, J = 2.7 Hz, 1 H, 4-H), 6.94 (d, J = 9.2 Hz, 1 H, 1-H), 3.98 (br. d, J = (−)13.0 Hz, 1 H, 10-H$_A$), 3.91 (dd, J = 11.6, 2.8 Hz, 1 H, 6a-H), 2.90 (m, J = (−)13.0, 13.0, 2.4 Hz, 1 H, 10-H$_B$), 2.06−1.34 (m, 6 H, 7-, 8-, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 166.2 (C-6), 140.3 (C-11a), 137.5 (C-3), 126.0 (C-4a), 120.2 (C-2), 110.3 (C-1), 109.5 (C-4), 59.1 (C-6a), 46.0 (C-10), 27.7 (C-7), 23.3, 22.9 (C-8, -9) ppm. EI MS: m/z (%) = 247 (83) [M$^+$], 218 (100), 200 (7), 190 (28), 172 (17), 163 (58), 144 (10), 133 (16), 117 (16), 105 (5), 90 (9). $C_{12}H_{13}N_3O_3$ (247.25): calcd. C 58.29, H 5.30, N 16.99; found C 58.36, H 5.50, N 17.09.

3-Nitro-6a,7-dihydro-5*H*-indolo[1,2-*a*]quinoxalin-6-one (37): Yield: 0.17 g (6%) (Method b); crystals of compound **37** (pyridine/water) decompose without melting above ca. 220 °C affording a copious sublimate of thin needles that was shown to be (TLC) dehydro derivative **56** (m.p. > 360 °C, see below). IR (nujol): $\tilde{\nu}$ = 1682 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 11.05 (br. s, 1 H, NH), 7.91 (dd, J = 9.0, 2.7 Hz, 1 H, 2-H), 7.80 (d, J = 2.7 Hz, 1 H, 4-H), 7.70 (d, J = 9.0 Hz, 1 H, 1-H), 7.33 (d, J = 7.5 Hz, 1 H, 11-H), 7.26 (d, J = 7.5 Hz, 1 H, 8-H), 7.17 (dd, J = 7.5, 7.5 Hz, 1 H, 10-H), 6.93 (dd, J = 7.5, 7.5 Hz, 1 H, 9-H), 4.78 (dd, J = 10.8, 9.3 Hz, 1 H, 6a-H), 3.44 (dd, J = (−)16.8, 9.3 Hz, 1 H, 7-H$_A$), 3.39 (dd, J = (−)16.8, 10.8 Hz, 1 H, 7-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 167.9 (C-6), 144.3 (C-11a), 141.1 (C-3), 136.0 (C-12a), 130.3 (C-4a), 130.0 (C-7a), 128.4 (C-10), 126.2 (C-8), 122.4 (C-9), 119.9 (C-2), 116.4 (C-1), 111.4 (C-4), 109.8 (C-11), 60.3 (C-6a), 30.2 (C-7) ppm. EI MS: m/z (%) = 281 (85) [M$^+$], 265 (3), 252 (100), 235 (7), 222 (11), 206 (52), 191 (6), 180 (11), 178 (13), 167 (4), 152 (6), 140 (4), 128 (5), 117 (8), 103 (9), 89 (17). $C_{15}H_{11}N_3O_3$ (281.3): calcd. C 64.05, H 3.94, N 14.94; found C 64.18, H 3.81, N 14.67.

3-Nitro-6a,7-dihydro-5*H*,12*H*-isoquinolino[2,3-*a*]quinoxalin-6-one (38): Yield: 1.77 g (60%) (Method b); crystals (pyridine/water) of compound **38** do not have a well-defined m.p.; they decompose with darkening from about 240 °C and their birefringence (polarized light, crossed nicols) is lost at ca. 280 °C. IR (nujol): $\tilde{\nu}$ = 1682 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.94 (br. s, 1 H, NH), 7.83 (dd, J = 9.2, 2.6 Hz, 1 H, 2-H), 7.66 (d, J = 2.6 Hz, 1 H, 4-H), 7.23 (m, 4 H, 8-, 9-, 10-, 11-H), 6.99 (d, J = 9.2 Hz, 1 H, 1-H), 4.95 (d, J = (−)17.1 Hz, 1 H, 12-H$_A$), 4.42 (d, J = (−)17.1 Hz, 1 H, 12-H$_B$), 4.40 (dd, J = 11.6, 3.9 Hz, 1 H, 6a-H), 3.24 (dd, J = (−)16.5, 3.9 Hz, 1 H, 7-H$_A$), 2.99 (dd, J = (−)16.5, 11.6 Hz, 1 H, 7-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 165.6 (C-6), 139.9 (C-13a), 137.9 (C-3), 132.4 (C-11a), 131.9 (C-7a), 128.8 (C-8), 126.6, 126.5, 126.3 (C-9, -10, -11), 125.8 (C-4a), 120.3 (C-2), 110.6 (C-1), 109.4 (C-4), 55.6 (C-6a), 47.9 (C-12), 31.1 (C-7) ppm. EI MS: m/z (%) = 295 (33) [M$^+$], 266 (2), 246 (3), 219 (3), 191 (2), 130 (2), 128 (2), 115 (7), 104 (100), 90 (4), 89 (3). $C_{16}H_{13}N_3O_3$ (295.3): calcd. C 65.08, H 4.44, N 14.23; found C 65.31, H 4.58, N 14.45.

***N*-Methoxyquinoxalinones 29−31:** These compounds were prepared from DNP-imino acids **7**, **8**, and **10** following Methods a$_1$ and a$_2$.

1-Methoxy-4-methyl-7-nitro-3,4-dihydro-1*H*-quinoxalin-2-one (29): Yield: 323 mg (45%) and 215 mg (30%) [from DNP-sarcosine (**7**), Methods a$_1$ and a$_2$, respectively]; m.p. 169−171 °C (decomp., ethanol). IR (KBr): $\tilde{\nu}$ = 1703 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.93 (dd, J = 9.0, 2.2 Hz, 1 H, 6-H), 7.74 (d, J = 2.2 Hz, 1 H, 8-H), 6.81 (d, J = 9.0 Hz, 1 H, 5-H), 4.22 (s, 2 H, 3-H), 3.89 (s, 3 H, OCH_3), 2.94 (s, 3 H, 4-CH_3) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 159.1 (C-2), 141.5 (C-4a), 137.4 (C-7), 125.0 (C-8a), 121.4 (C-6), 110.2 (C-5), 106.2 (C-8), 62.5 (OCH_3), 53.8 (C-3), 36.8 (4-CH_3) ppm. EI MS: m/z (%) = 237 (21) [M$^+$], 206 (39), 178 (19), 160 (33), 132 (100), 120 (6), 117 (6), 104 (7), 90 (8). $C_{10}H_{11}N_3O_4$ (237.2): calcd. C 50.63, H 4.67, N 17.71; found C 50.51, H 4.61, N 17.56.

(*S*)-5-Methoxy-7-nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (30): Yield: 220 mg (25%) and 219 mg (25%) [from

DNP-L-proline (**8**), Methods a$_1$ and a$_2$, respectively]; m.p. 155−157 °C (decomp., ethanol). $[\alpha]_D^{22} = -612.3$ ($c = 0.1$, MeOH). IR (KBr): $\tilde{\nu} = 1683$ (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.94 (dd, J = 9.0, 2.6 Hz, 1 H, 8-H), 7.73 (d, J = 2.6 Hz, 1 H, 6-H), 6.69 (d, J = 9.0 Hz, 1 H, 9-H), 4.34 (dd, J = 9.1, 6.1 Hz, 1 H, 3a-H), 3.87 (s, 3 H, OCH$_3$), 3.46 (m, 2 H, 1-H), 2.23 (m, 1 H, 3-H$_A$), 2.03 (m, 3 H, 2-H, 3-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 159.9 (C-4), 139.5 (C-9a), 137.1 (C-7), 125.3 (C-5a), 121.7 (C-8), 110.5 (C-9), 106.6 (C-6), 62.5 (OCH$_3$), 60.3 (C-3a), 46.7 (C-1), 27.6 (C-3), 21.8 (C-2) ppm. EI MS: m/z (%) = 263 (26) [M$^+$], 232 (75), 204 (39), 186 (88), 174 (7), 158 (100), 146 (11), 144 (11), 130 (24), 117 (14), 116 (14), 103 (17), 89 (17). $C_{12}H_{13}N_3O_4$ (263.25): calcd. C 54.75, H 4.98, N 15.96; found C 54.65, H 4.77, N 15.87.

5-Methoxy-3-nitro-7,8,9,10-tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (31): Yield: 220 mg (29%) and 307 mg (40%) [from DNP-DL-pipecolic acid (**10**), Methods a$_1$ and a$_2$, respectively]; m.p. 168−170 °C (decomp., 1-propanol). IR (KBr): $\tilde{\nu} = 1690$ (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.92 (dd, J = 9.1, 2.6 Hz, 1 H, 2-H), 7.76 (d, J = 2.6 Hz, 1 H, 4-H), 7.03 (d, J = 9.1 Hz, 1 H, 1-H), 4.13 (dd, J = 11.4, 2.9 Hz, 1 H, 6a-H), 3.96 (br. d, J = (−)13.0 Hz, 1 H, 10-H$_A$), 3.88 (s, 3 H, OCH$_3$), 2.91 (m, J = (−)13.0, 13.0, 2.6 Hz, 1 H, 10-H$_B$), 2.06−1.42 (m, 6 H, 7-, 8-, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 161.6 (C-6), 140.4 (C-11a), 138.0 (C-3), 125.2 (C-4a), 121.3 (C-2), 111.2 (C-1), 106.4 (C-4), 62.6 (OCH$_3$), 60.2 (C-6a), 46.1 (C-10), 27.8 (C-7), 23.0, 22.8 (C-8, -9) ppm. EI MS: m/z (%) = 277 (24) [M$^+$], 246 (100), 218 (32), 200 (67), 172 (80), 144 (21), 131 (13), 130 (13), 117 (16), 116 (16), 104 (10), 103 (10), 89 (16). $C_{13}H_{15}N_3O_4$ (277.3): calcd. C 56.31, H 5.45, N 15.15; found C 56.60, H 5.67, N 15.31.

***N*-Methylquinoxalinones 45−49:** These compounds were prepared from DNP-imino acids **7**, **8**, and **10** following Method a$_2$ or by methylation of isolated quinoxalinones **33**−**36** and **38** according to the following procedure: Methyl iodide (2 mL, excess) was added to a suspension of the corresponding quinoxalinone (5 mmol) and potassium carbonate (1.38 g, 10 mmol) in acetone (50 mL) and the mixture was heated in an autoclave at 80−90 °C with stirring for 3 h. After cooling, the solvent was evaporated to dryness and, after addition of water (50 mL), the methylated product was extracted with chloroform (3 × 40 mL). The solution was dried with magnesium sulfate and the solvent was evaporated to afford the desired compounds as practically pure (^{1}H NMR) solids that were recrystallized from the appropriate solvent.

1,4-Dimethyl-7-nitro-3,4-dihydro-1*H*-quinoxalin-2-one (45): Yield: 110 mg (16%) [from DNP-sarcosine (**7**), Method a$_2$], 0.96 g (87%) (from quinoxalinone **33**); m.p. 165−167 °C (decomp., ethanol), ref.[5] m.p. 165−168 °C.

(*S*)-5-Methyl-7-nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (46): Yield: 190 mg (23%) [from DNP-L-proline (**8**), Method a$_2$], 1.01 g (82%) (from quinoxalinone **34**); m.p. 194−197 °C (decomp., 1-propanol). $[\alpha]_D^{22} = -460.5$ ($c = 0.1$, MeOH). IR (KBr): $\tilde{\nu} = 1670$ (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.93 (dd, J = 8.8, 2.2 Hz, 1 H, 8-H), 7.73 (d, J = 2.2 Hz, 1 H, 6-H), 6.68 (d, J = 8.8 Hz, 1 H, 9-H), 4.06 (dd, J = 9.2, 6.2 Hz, 1 H, 3a-H), 3.47 (m, 2 H, 1-H), 3.33 (s, 3 H, CH$_3$), 2.25 (m, 1 H, 3-H$_A$), 2.00 (m, 3 H, 2-H, 3-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 165.0 (C-4), 141.2 (C-9a), 137.2 (C-7), 128.5 (C-5a), 120.9 (C-8), 110.0 (C-9), 109.6 (C-6), 58.9 (C-3a), 46.6 (C-1), 28.5 (CH$_3$), 27.9 (C-3), 21.7 (C-2) ppm. EI MS: m/z (%) = 247 (74) [M$^+$], 218 (24), 200 (10), 191 (100), 172 (12), 145 (30), 131 (11), 130 (10), 117 (8), 104 (13), 91 (20). $C_{12}H_{13}N_3O_3$ (247.25): calcd. C 58.29, H 5.30, N 16.99; found C 58.10, H 5.50, N 16.80.

5-Methyl-7-nitro-1,2,3,3a-tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (47): Yield: 1.04 g (84%) (from quinoxalinone **35**); m.p. 198−201 °C (decomp., 1-propanol). IR (KBr): $\tilde{\nu} = 1675$ (CO) cm^{-1}. Other spectroscopic data are identical to those of S enantiomer **46**. $C_{12}H_{13}N_3O_3$ (247.25): calcd. C 58.29, H 5.30, N 16.99; found C 58.04, H 5.05, N 16.87.

5-Methyl-3-nitro-7,8,9,10-tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (48): Yield: 122 mg (17%) [from DNP-DL-pipecolic acid (**10**), Method a$_2$], 1.10 g (84%) (from quinoxalinone **36**); m.p. 180−182 °C (decomp., ethanol). IR (nujol): $\tilde{\nu} = 1678$ (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.92 (dd, J = 9.2, 2.6 Hz, 1 H, 2-H), 7.73 (d, J = 2.6 Hz, 1 H, 4-H), 7.03 (d, J = 9.2 Hz, 1 H, 1-H), 3.98 (m, 2 H, 6a-H, 10-H$_A$), 3.33 (s, 3 H, CH$_3$), 2.94 (m, J = (−)12.8, 12.8, 2.9 Hz, 1 H, 10-H$_B$), 2.06−1.37 (m, 6 H, 7-, 8-, 9-H) ppm. ^{1}H NMR (CDCl$_3$): δ = 3.89 (br. d, J = (−)13.0 Hz, 1 H, 10-H$_A$), 3.80 (dd, J = 11.2, 3.1 Hz, 1 H, 6a-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 165.9 (C-6), 141.9 (C-11a), 138.0 (C-3), 128.2 (C-4a), 120.6 (C-2), 110.9 (C-1), 109.5 (C-4), 59.2 (C-6a), 46.2 (C-10), 28.6 (CH$_3$), 27.7 (C-7), 23.1, 22.6 (C-8, -9) ppm. EI MS: m/z (%) = 261 (100) [M$^+$], 232 (84), 204 (31), 186 (18), 177 (97), 158 (14), 147 (24), 131 (35), 116 (8), 104 (15), 91 (18). $C_{13}H_{15}N_3O_3$ (261.3): calcd. C 59.76, H 5.79, N 16.08; found C 59.47, H 5.58, N 15.79.

5-Methyl-3-nitro-6a,7-dihydro-5*H*,12*H*-isoquinolino[2,3-*a*]quinoxalin-6-one (49): Yield: 1.35 g (87%) (from quinoxalinone **38**); m.p. 210−213 °C (decomp., *n*-butanol). IR (nujol): $\tilde{\nu} = 1676$ (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 7.94 (dd, J = 9.0, 2.4 Hz, 1 H, 2-H), 7.77 (d, J = 2.4 Hz, 1 H, 4-H), 7.25 (m, 4 H, 8-, 9-, 10-, 11-H), 7.06 (d, J = 9.0 Hz, 1 H, 1-H), 4.97 (d, J = (−)16.8 Hz, 1 H, 12-H$_A$), 4.51 (dd, J = 11.6, 4.0 Hz, 1 H, 6a-H), 4.47 (d, J = (−)16.8 Hz, 1 H, 12-H$_B$), 3.40 (s, 3 H, CH$_3$), 3.22 (dd, J = (−)16.3, 4.0 Hz, 1 H, 7-H$_A$), 2.97 (dd, J = (−)16.3, 11.6 Hz, 1 H, 7-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 165.3 (C-6), 141.2 (C-13a), 138.3 (C-3), 132.3 (C-11a), 131.9 (C-7a), 128.8 (C-8), 128.0 (C-4a), 126.7, 126.51, 126.47 (C-9, -10, -11), 120.7 (C-2), 111.1 (C-1), 109.5 (C-4), 56.0 (C-6a), 48.0 (C-12), 30.8 (C-7), 28.7 (CH$_3$) ppm. EI MS: m/z (%) = 309 (19) [M$^+$], 293 (1), 279 (4), 260 (1), 233 (1), 218 (1), 205 (1), 175 (3), 147 (4), 131 (3), 115 (6), 104 (100), 91 (3). $C_{17}H_{15}N_3O_3$ (309.3): calcd. C 66.01, H 4.89, N 13.58; found C 65.93, H 4.69, N 13.42.

Preparation of Aminoquinoxalinones 54 and 55: These compounds were prepared from DNP-imino acids esters **13** and **14**, respectively, following Method c$_1$ or by other alternative methods described below.

7-Amino-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (54): Yield: 0.59 g (58%) (Method c$_1$). This compound was also prepared alternatively as follows: A mixture of compound **34** (0.50 g, 2.1 mmol), cyclohexene (2 mL) and 10% Pd/C (1.70 g) in ethanol (20 mL) was heated under reflux for 3 h. After cooling, the catalyst was removed by filtration and the cake washed with pyridine (3 × 5 mL). After evaporation of the combined solvents, column chromatography of the residue using chloroform/methanol (50:1 to 10:1) mixtures afforded the desired compound (0.29 g, 68%). Similar results were obtained starting from racemic nitroquinoxalinone **35**. M.p. 323−325 °C (decomp., 1,4-dioxane). IR (nujol): $\tilde{\nu} = 3457$, 3370 (NH$_2$), 1675 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.94 (br. s, 1 H, NH), 7.92 (dd, J = 2.7, 1.5 Hz, 1 H, 1-H), 7.67 (d, J = 8.6 Hz, 1 H, 9-H), 6.89 (dd, J = 3.8, 1.5 Hz, 1 H, 3-H), 6.54 (dd, J = 3.8, 2.7 Hz, 1 H, 2-H), 6.46 (d, J = 2.3 Hz, 1 H, 6-H), 6.43 (dd, J = 8.6, 2.3 Hz, 1 H, 8-H), 5.28 (br. s, 2 H, NH$_2$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 155.5 (C-4), 147.0 (C-7), 129.5 (C-5a), 122.3 (C-

3a), 116.7 (C-1), 115.6 (C-9), 113.5 (C-9a), 111.6 (C-2), 110.2 (C-3), 109.3 (C-8), 99.8 (C-6) ppm. EI MS: *m*/*z* (%) = 199 (100) [M$^+$], 170 (18), 155 (3), 144 (16), 117 (10), 105 (3), 91 (3), 90 (3), 89 (3). $C_{11}H_9N_3O$ (199.2): calcd. C 66.32, H 4.55, N 21.09; found C 66.50, H 4.67, N 20.96.

3-Amino-7,8,9,10-tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (55): Yield: 0.46 g (66%) (Method c$_1$). This compound was also prepared alternatively as follows: A solution of nitro compound **36** (0.50 g, 2.0 mmol) in pyridine (40 mL) was hydrogenated in the presence of 10% Pd/C (50 mg) at 15 psi for 1 h. The catalyst was removed and the solvent evaporated to dryness. After addition of water (5 mL), the solid in suspension was collected by filtration affording pure (^{1}H NMR) amine **55** (0.39 g, 89%). M.p. 198−200 °C (decomp.); a product claimed to be amine **55** has been described by Adegoke and Alo[18] but the reported m.p. (180−182 °C), as well as the ^{1}H NMR spectrum, are rather different from those found by us. IR (nujol): ṽ = 3411, 3308 (NH$_2$), 1687 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.15 (br. s, 1 H, NH), 6.52 (d, *J* = 9.2 Hz, 1 H, 1-H), 6.15 (m, 2 H, 2-, 4-H), 4.59 (br. s, 2 H, NH$_2$), 3.51 (br. d, *J* = (−)12.0 Hz, 1 H, 10-H$_A$), 3.10 (m, 1 H, 6a-H), 2.42 (m, 1 H, 10-H$_B$), 2.00 (m, 1 H, 7-H$_A$), 1.85−1.19 (m, 5 H, 7-H$_B$, 8-, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 168.6 (C-6), 142.0 (C-3), 128.1 (C-4a), 126.7 (C-11a), 113.2 (C-1), 108.6 (C-2), 101.9 (C-4), 59.2 (C-6a), 46.8 (C-10), 26.4 (C-7), 23.5, 23.0 (C-8, -9) ppm. EI MS: *m*/*z* (%) = 217 (70) [M$^+$], 188 (69), 160 (23), 146 (9), 133 (100), 105 (12), 92 (3).

Free compound **55** is very air-sensitive, becoming dark very quickly when exposed to air, especially in solution; for characterization purposes, the crude product was triturated with a saturated solution of oxalic acid in ethanol (10 mL), affording a white precipitate of the corresponding oxalate, which was isolated by filtration, washed with cold ethanol and dried under vacuum. **55** Oxalate: m.p. 205−207 °C (decomp.). $C_{12}H_{15}N_3O{\cdot}C_2O_4H_2$ (307.3): calcd. C 54.72, H 5.58, N 13.67; found C 54.50, H 5.71, N 13.51.

Preparation of *N*-(2-Nitrophenyl)imino Acids 15−20: Compounds **15**−**18** were prepared from the corresponding *N*-alkylamino or cyclic imino acids (18 mmol), 1-fluoro-2-nitrobenzene (2.82 g, 20 mmol), and sodium hydrogencarbonate (3.78 g, 45 mmol) in refluxing ethanol/water (1:1, 200 mL), following the procedure of Goudie and Preston.[19] After acidification, the desired compounds were extracted with chloroform; evaporation of the solvent yielded practically pure products (TLC, ^{1}H NMR) that were used directly in further steps. Compounds **16** and **18** were orange oils that solidified very slowly on standing. NP-sarcosine (**15**): 92% yield, m.p. 93−95 °C (carbon tetrachloride), ref.[19] 75 °C, ref.[35] 88−92 °C; NP-L-proline (**16**): 94% yield, m.p. 83−85 °C (solidified oil), ref.[19] 57 °C, ref.[18] oil; NP-DL-pipecolic acid (**18**): 91% yield, m.p. 81−83 °C (carbon tetrachloride), ref.[30] 79−80 °C.

The method described above does not proceed well for compounds **19** and **20**, which were prepared as follows: A well-stirred mixture of the corresponding imino acid (indoline-2-carboxylic acid or 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride) (10 mmol), 1-fluoro-2-nitrobenzene (1.69 g, 12 mmol) and potassium carbonate (4.84 g, 35 mmol) in dimethyl sulfoxide (30 mL) was heated for 24 h at 95−100 °C (for **19**) or at 75−80 °C (for **20**). After cooling, the resulting suspension was poured in water (300 mL) and extracted with diethyl ether (3 × 50 mL). The water phase was acidified at pH 1 with dil. hydrochloric acid and the precipitated gum, which solidified on standing, was collected by filtration, washed with water and air-dried.

***N*-(2-Nitrophenyl)-DL-proline (17):** Yield: 3.95 g (93%); m.p. 116−118 °C (carbon tetrachloride). IR (KBr): ṽ = 1716 (CO) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 7.71 (dd, *J* = 8.2, 1.5 Hz, 1 H, 3′-H), 7.37 (m, *J* = 8.6, 7.1, 1.6 Hz, 1 H, 5′-H), 6.85 (m, 2 H, 4′-, 6′-H), 4.41 (t, *J* = 7.0 Hz, 1 H, 2-H), 3.51 (m, 1 H, 5-H$_A$), 3.04 (m, 1 H, 5-H$_B$), 2.47 (m, 1 H, 3-H$_A$), 2.25−1.80 (m, 3 H, 3-H$_B$, 4-H) ppm. (This ^{1}H NMR spectrum is identical to that recorded by us for the corresponding L-proline derivative **16**, but rather different, however, from that reported[18] by Adegoke and Alo for the latter.) ^{13}C NMR (CDCl$_3$): δ = 178.3 (CO), 141.2 (C-1′), 138.7 (C-2′), 133.1 (C-5′), 126.5 (C-3′), 118.0 (C-4′), 116.7 (C-6′), 61.6 (C-2), 51.7 (C-5), 30.9 (C-3), 24.7 (C-4) ppm. EI MS: *m*/*z* (%) = 236 (6) [M$^+$], 219 (1), 191 (100), 175 (10), 157 (24), 144 (64), 131 (12), 130 (10), 117 (28), 104 (41), 91 (19). $C_{11}H_{12}N_2O_4$ (236.2): calcd. C 55.93, H 5.12, N 11.86; found C 56.11, H 5.08, N 12.04.

1-(2-Nitrophenyl)indoline-2-carboxylic Acid (19): Yield: 2.13 g (75%); an analytical sample was prepared according to the method described above for the corresponding 2,4-dinitrophenyl analogue **11**; m.p. 107−108 °C (decomp.). IR (KBr): ṽ = 1725 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 8.00 (d, *J* = 7.9 Hz, 1 H, 3′-H), 7.74 (dd, *J* = 7.9, 7.9 Hz, 1 H, 5′-H), 7.60 (d, *J* = 7.9 Hz, 1 H, 6′-H), 7.41 (dd, *J* = 7.9, 7.9 Hz, 1 H, 4′-H), 7.16 (d, *J* = 7.4 Hz, 1 H, 4-H), 6.96 (dd, *J* = 7.4, 7.4 Hz, 1 H, 6-H), 6.74 (dd, *J* = 7.4, 7.4 Hz, 1 H, 5-H), 6.20 (d, *J* = 7.4 Hz, 1 H, 7-H), 4.90 (dd, *J* = 10.3, 7.3 Hz, 1 H, 2-H), 3.56 (dd, *J* = (−)15.9, 10.3 Hz, 1 H, 3-H$_A$), 3.20 (dd, *J* = (−)15.9, 7.3 Hz, 1 H, 3-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 172.7 (CO), 148.0 (C-7a), 145.6 (C-2′), 136.6 (C-1′), 134.4 (C-5′), 128.0 (C-3a), 127.5 (C-6′), 127.2 (C-6), 125.9 (C-4′), 125.6 (C-3′), 124.7 (C-4), 119.6 (C-5), 107.4 (C-7), 66.0 (C-2), 33.2 (C-3) ppm. EI MS: *m*/*z* (%) = 284 (30) [M$^+$], 239 (58), 221 (12), 205 (45), 194 (67), 191 (66), 180 (100), 165 (32), 152 (12), 139 (12), 115 (8), 103 (8), 102 (8), 89 (35). $C_{15}H_{12}N_2O_4$ (284.3): calcd. C 63.38, H 4.25, N 9.85; found C 63.45, H 4.21, N 9.72.

2-(2-Nitrophenyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (20): Yield: 2.56 g (86%); m.p. 144−146 °C (decomp., carbon tetrachloride). IR (KBr): ṽ = 1699 (CO) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 7.83 (dd, *J* = 8.2, 1.6 Hz, 1 H, 3′-H), 7.50 (m, *J* = 8.3, 7.2, 1.6 Hz, 1 H, 5′-H), 7.35 (dd, *J* = 8.3, 1.2 Hz, 1 H, 6′-H), 7.17 (m, 3 H) and 7.04 (m, 1 H) (5-, 6-, 7-, 8-H), 7.10 (m, *J* = 8.2, 7.2, 1.2 Hz, 1 H, 4′-H), 4.79 (d, *J* = (−)15.4 Hz, 1 H, 1-H$_A$), 4.33 (dd, *J* = 6.3, 2.7 Hz, 1 H, 3-H), 4.09 (d, *J* = (−)15.4 Hz, 1 H, 1-H$_B$), 3.49 (dd, *J* = (−)16.1, 6.3 Hz, 1 H, 4-H$_A$), 3.23 (dd, *J* = (−)16.1, 2.7 Hz, 1 H, 4-H$_B$) ppm. ^{13}C NMR (CDCl$_3$): δ = 176.7 (CO), 144.6 (C-1′), 143.1 (C-2′), 133.8 (C-5′), 132.5, 131.7 (C-4a, -8a), 128.8, 126.8, 126.5, 126.2 (two superimposed signals) (C-5, -6, -7, -8, -3′), 123.1 (C-6′), 122.8 (C-4′), 60.0 (C-3), 49.4 (C-1), 30.5 (C-4) ppm. EI MS: *m*/*z* (%) = 298 (0.8) [M$^+$], 297 (1.5), 281 (48), 264 (18), 253 (53), 250 (35), 236 (35), 235 (33), 219 (100), 206 (48), 178 (7), 165 (3), 128 (13), 115 (9), 103 (17), 91 (7). $C_{16}H_{14}N_2O_4$ (298.3): calcd. C 64.42, H 4.73, N 9.39; found C 64.25, H 4.62, N 9.18.

Reduction/Cyclization of *N*-(2-Nitrophenyl)imino Acids and Their Methyl Esters to Quinoxalinones 39−44

Method d. Hydrogenation of *N*-(2-Nitrophenyl)imino Acids 15−18 and Their Methyl Esters 21−24: A solution of the corresponding NP-imino acid (**15**−**18**) (Method d$_1$) or their methyl esters [**21**−**24**; 10 mmol; prepared by sulfuric acid-catalyzed esterification of the acids (Method d$_2$)][18,30] in ethanol (100 mL) was hydrogenated at 30 °C and 20 psi in the presence of 10% Pd/C. Under these conditions, L- and DL-proline-derived acids **16** and **17**, as well as esters **21**−**24**, were completely converted into the corresponding quinoxalinones within 1−2 h; nevertheless, NP-sarcosine (**15**) and NP-pipecolic acid (**18**) gave mixtures of the desired quinoxalinones **39** and **42** together with the corresponding *N*-hydroxy derivatives [ca.

15% and ca. 45%, respectively, as determined by ^{1}H NMR spectroscopy (molar ratios)]. The latter were hydrogenolyzed rather slowly to the corresponding quinoxalinones, usually with 4−7 d being required to complete the reaction under the described hydrogenation conditions. In all cases, when the reaction was finished, 10% aq. sodium metabisulfite solution (1 mL) was added to prevent oxidation of the oxygen-sensitive quinoxalinones, the catalyst was removed by filtration, and the solution was evaporated to dryness. The residue was triturated with cold water (10 mL) and the solid in suspension was collected by filtration, washed with water, and dried. In the case of the rather-water-soluble 4-methyl derivative **39**, extraction of the filtrate with chloroform afforded an additional significant amount of product. Quinoxalinones prepared from esters contained some impurities (^{1}H NMR) that decompose when exposed to air affording dark crude products; these impurities were not present in crude quinoxalinones arising from acids.

Method e. Treatment of *N*-(2-Nitrophenyl)-L-proline Methyl Ester (22) with Cyclohexene−5% Pd/C: Starting from methyl ester **22** (0.40 g, 1.6 mmol), initially we followed the procedure described by Alo et al.[30] for the cyclization of pipecolic acid-derived analogue **24**. Isolation of the corresponding quinoxalinone **40** was carried out as described in Method d, including treatment with sodium metabisulfite; otherwise an intensely green-colored compound was obtained. The (*S*)-quinoxalinone **40** thus isolated was partially racemized.

Method f. Treatment of *N*-(2-Nitrophenyl)imino Acids 15−20 with Sodium Dithionite: A solution of the corresponding NP-imino acid (**15**−**20**) (10.0 mmol) and potassium carbonate (1.41 g, 10.2 mmol) in water (30 mL) was added portionwise to a well-stirred solution of sodium dithionite (10.45 g, 60.0 mmol) in water (60 mL). After 30 min the precipitated solid was collected by filtration, washed with water and air-dried. As in Method d, an additional significant amount of the rather-water-soluble 4-methyl derivative **39** was obtained by extraction of the filtrate with chloroform.

4-Methyl-3,4-dihydro-1*H*-quinoxalin-2-one (39): Yield: 1.41 g (87%) (Methods d$_1$ and d$_2$), 1.35 g (83%) (Method f); m.p. 140−142 °C (decomp., water), ref.[5] m.p. 140−143 °C.

(*S*)-1,2,3,3a-Tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (40): Yield: 1.58 g (84%) (Method d$_1$) (sometimes a slightly racemized material, ≥ 90% *ee*), 1.62 g (86%) (Method d$_2$) (sometimes a slightly racemized material, ≥ 90% *ee*), 0.23 g (76%) (Method e) (partially racemized material, 50−70% *ee*), 1.64 g (87%) (Method f) (enantiomerically pure material); m.p. 163−165 °C (decomp., ethanol/water), ref.[18] 174−175 °C (practically identical to that reported[33] for the corresponding racemic compound **41**, see below). $[\alpha]_{D}^{22} = -82.6$ (c = 0.1, MeOH). IR (KBr): $\tilde{\nu}$ = 1684 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.33 (br. s, 1 H, NH), 6.87 (m, J = 7.6, 7.6, 1.5 Hz, 1 H, 8-H), 6.81 (dd, J = 7.6, 1.5 Hz, 1 H, 6-H), 6.68 (m, J = 7.6, 7.6, 1.3 Hz, 1 H, 7-H), 6.57 (d, J = 7.6 Hz, 1 H, 9-H), 3.53 (dd, J = 8.6, 6.8 Hz, 1 H, 3a-H), 3.39 (m, 1 H, 1-H$_A$), 3.04 (m, 1 H, 1-H$_B$), 2.10 (m, 1 H, 3-H$_A$), 1.93 (m, 3 H, 2-H, 3-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 167.6 (C-4), 135.3 (C-9a), 128.1 (C-5a), 123.1 (C-8), 118.4 (C-7), 114.8 (C-6), 112.0 (C-9), 59.7 (C-3a), 46.2 (C-1), 26.4 (C-3), 21.7 (C-2) ppm. EI MS: m/z (%) = 188 (50) [M^{+}], 159 (28), 132 (100), 118 (12), 104 (6), 90 (6). C$_{11}$H$_{12}$N$_2$O (188.2): calcd. C 70.19, H 6.43, N 14.88; found C 70.01, H 6.66, N 15.11.

1,2,3,3a-Tetrahydro-5*H*-pyrrolo[1,2-*a*]quinoxalin-4-one (41): Yield: 1.69 g (90%) (Method d$_1$), 1.73 g (92%) (Methods d$_2$ and f); m.p. 175−177 °C (decomp., ethanol/water), ref.[33] 174.5−176 °C. IR (KBr): $\tilde{\nu}$ = 1684 (CO) cm^{-1}. Other spectroscopic data are identical to those of *S* enantiomer **40**.

7,8,9,10-Tetrahydro-5*H*,6a*H*-pyrido[1,2-*a*]quinoxalin-6-one (42): Yield: 1.84 g (91%) (Method d$_1$), 1.82 g (90%) (Method d$_2$), 1.68 g (83%) (Method f); m.p. 192−194 °C (decomp., benzene/cyclohexane), ref.[30] 189−190 °C and 190−191 °C, ref.[18] 148−149 °C. IR (KBr): $\tilde{\nu}$ = 1678 (CO) cm^{-1}. ^{1}H NMR spectrum ([D$_6$]DMSO) is identical to that reported[30] by Alo et al., but EI MS is rather different from that described[18] by Adegoke and Alo. ^{13}C NMR ([D$_6$]DMSO): δ = 167.8 (C-6), 135.4 (C-11a), 127.1 (C-4a), 123.1 (C-2), 118.9 (C-3), 114.8 (C-4), 112.1 (C-1), 58.8 (C-6a), 46.0 (C-10), 26.5 (C-7), 23.1, 23.0 (C-8, -9) ppm. EI MS: m/z (%) = 202 (58) [M^{+}], 173 (88), 145 (38), 131 (11), 118 (100), 91 (9).

6a,7-Dihydro-5*H*-indolo[1,2-*a*]quinoxalin-6-one (43): Yield: 1.65 g (70%) (Method f). Crystals (ethanol) of compound **43** melt partially at 205−210 °C and then resolidify showing a further m.p. at 327−330 °C (decomp.); a TLC study of the process shows that when heated compound **43** is oxidized by air to dehydro derivative **57** [m.p. 328−331 °C (decomp.), see below]. IR (KBr): $\tilde{\nu}$ = 1682 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.63 (br. s, 1 H, NH), 7.46 (dd, J = 7.1, 2.0 Hz, 1 H, 1-H), 7.18 (d, J = 7.2 Hz, 1 H, 8-H), 7.07 (m, 3 H, 2-, 3-, 10-H), 7.00 (dd, J = 7.3, 2.0 Hz, 1 H, 4-H), 6.94 (d, J = 7.9 Hz, 1 H, 11-H), 6.77 (dd, J = 7.2, 7.2 Hz, 1 H, 9-H), 4.55 (dd, J = 10.8, 5.1 Hz, 1 H, 6a-H), 3.56 (dd, J = (−)16.5, 5.1 Hz, 1 H, 7-H$_A$), 3.34 (dd, J = (−)16.5, 10.8 Hz, 1 H, 7-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 168.1 (C-6), 146.5 (C-11a), 130.5 (C-4a), 128.8 (C-12a), 127.43 (C-7a), 127.40 (C-10), 124.9 (C-8),123.4 (C-3), 122.7 (C-2), 120.3 (C-1), 119.7 (C-9), 116.2 (C-4), 106.9 (C-11), 59.8 (C-6a), 29.6 (C-7) ppm. EI MS: m/z (%) = 236 (50) [M^{+}], 207 (100), 180 (6), 152 (4), 118 (10), 103 (17), 89 (12). C$_{15}$H$_{12}$N$_2$O (236.3): calcd. C 76.25, H 5.12, N 11.86; found C 76.01, H 5.33, N 12.06.

6a,7-Dihydro-5*H*,12*H*-isoquinolino[2,3-*a*]quinoxalin-6-one (44): Yield: 1.98 g (79%) (Method f). Crystals (from 2-propanol) of compound **44** melt partially at 245−248 °C and then resolidify and become dark from about 250 °C and then soften and char progressively without showing a well-defined m.p.; birefringence is completely lost at ca. 295−300 °C. IR (nujol): $\tilde{\nu}$ = 1692 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.54 (br. s, 1 H, NH), 7.28 (d, J = 7.3 Hz, 1 H, 11-H), 7.18 (m, 3 H, 8-, 9-, 10-H), 6.86 (m, 3 H, 1-, 2-, 4-H), 6.74 (m, J = 7.8, 6.6, 2.1 Hz, 1 H, 3-H), 4.77 (d, J = (−)16.6 Hz, 1 H, 12-H$_A$), 4.21 (d, J = (−)16.6 Hz, 1 H, 12-H$_B$), 4.08 (dd, J = 11.6, 4.2 Hz, 1 H, 6a-H), 3.12 (dd, J = (−)16.6, 4.2 Hz, 1 H, 7-H$_A$), 2.87 (dd, J = (−)16.6, 11.6 Hz, 1 H, 7-H$_B$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 166.7 (C-6), 133.7 (C-13a), 132.3, 132.1 (C-7a, -11a), 126.4 (C-4a), 128.3, 126.0, 125.8, 125.7 (C-8, -9, -10, -11), 122.7 (C-2), 118.6 (C-3), 114.3 (C-4), 112.1 (C-1), 55.5 (C-6a), 47.6 (C-12), 29.1 (C-7) ppm. EI MS: m/z (%) = 250 (44) [M^{+}], 221 (21), 146 (2), 124 (4), 118 (7), 104 (100), 91 (7). C$_{16}$H$_{14}$N$_2$O (250.3): calcd. C 76.78, H 5.64, N 11.19; found C 76.75, H 5.90, N 11.08.

Dehydrogenation of Quinoxalinones 5, 37, and 43 to Quinoxalinones 6, 56, and 57, respectively: Dehydrogenation reactions were carried out by means of iron(III) chloride or manganese(IV) oxide; in each case, however, the precise experimental conditions depend on the properties (solubility, etc.) of reactants and products.

With iron(III) chloride: For quinoxalinone **57**, iron(III) chloride hexahydrate (0.50 g, excess) was added to a stirred solution of the corresponding dihydro derivative **43** (120 mg, 0.51 mmol) in dimethyl sulfoxide (3 mL) and, after 12 h, a further portion of iron salt (0.20 g) was added. The dehydrogenation was complete after ca. 6 h (TLC) and then, after addition of water (20 mL), the precipitated solid was collected by filtration, washed with water (3 × 5 mL) and air-dried.

With manganese(IV) oxide: For quinoxalinone **6**, manganese(IV) oxide (5 g, excess) was added portionwise over 1 h to a solution of compound **5** (0.32 g, 1.0 mmol) in chloroform (50 mL). After 1 h the reaction was complete (TLC) and the inorganic material was removed by filtration. The solution obtained was concentrated and, to remove a low-R_f by-product,[36] it was percolated through a short silica gel column that was eluted with a chloroform/ethanol (100:1) mixture. Evaporation of the corresponding fractions afforded pure quinoxalinone **6**.

For quinoxalinone **56**, manganese(IV) oxide (0.50 g, excess) was added to a stirred solution of dihydro derivative **37** (141 mg, 0.50 mmol) in pyridine (40 mL). After 2 h, a further portion of manganese(IV) oxide (0.5 g) was added and the stirring was followed for 1 h. Inorganic material was then removed by filtration and the filtrate evaporated to dryness. The residue was triturated with water (10 mL) and the solid in suspension was collected by filtration, washed with water (3 × 5 mL), and air-dried.

For quinoxalinone **57**, manganese(IV) oxide (0.50 g, excess) was added to a stirred solution of dihydro derivative **43** (120 mg, 0.51 mmol) in chloroform (40 mL). When the reaction was complete (TLC, ca. 30 min), the suspension was evaporated to dryness and the solid obtained was extracted with boiling acetic acid (5 × 5 mL). Evaporation of acetic acid, addition of water (10 mL) and trituration yielded a solid that was collected by filtration, washed with water (3 × 5 mL), and air-dried.

5-Methyl-3-nitro-12,13-dihydro-5*H*-[3]benzazepino[3,2-*a*]quinoxalin-6-one (6): Yield: 0.25 g (78%); m.p. 217−219 °C (*n*-butanol). IR (KBr): $\tilde{\nu}$ = 1655 (CO) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 8.04 (dd, *J* = 9.0, 2.2 Hz, 1 H, 2-H), 7.91 (d, *J* = 2.2 Hz, 1 H, 4-H), 7.46 (d, *J* = 7.6 Hz, 1 H, 8-H), 7.27 (m, 1 H, 9-H), 7.21 (m, 2 H, 10-, 11-H), 7.14 (s, 1 H, 7-H), 6.95 (d, *J* = 9.0 Hz, 1 H, 1-H), 3.93 (m, 2 H, 13-H), 3.61 (s, 3 H, CH$_3$), 3.30 (m, 2 H, 12-H) ppm. ^{13}C NMR (CDCl$_3$): δ = 160.4 (C-6), 140.8 (C-3), 138.6 (C-11a), 136.7 (C-14a), 133.6 (C-8), 133.1 (C-7a), 129.5 (two superimposed signals, C-6a, -11), 129.0 (C-4a), 127.1 (C-10), 126.9 (C-9), 120.3 (C-2), 113.9 (C-7), 109.9 (C-4), 109.4 (C-1), 48.6 (C-13), 36.5 (C-12), 30.0 (CH$_3$) ppm. EI MS: *m/z* (%) = 321 (100) [M$^+$], 306 (36), 292 (5), 275 (11), 260 (32), 247 (10), 231 (15), 217 (8), 204 (8), 190 (4), 178 (4), 155 (7), 140 (6), 128 (30), 115 (55), 102 (11), 91 (12). $C_{18}H_{15}N_3O_3$ (321.3): calcd. C 67.28, H 4.71, N 13.08; found C 67.53, H 4.83, N 12.95.

3-Nitro-5*H*-indolo[1,2-*a*]quinoxalin-6-one (56): Yield: 116 mg (83%); m.p. > 360 °C (acetic acid). The compound sublimes from about 220 °C giving thin yellow needles. IR (nujol): $\tilde{\nu}$ = 1690 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 11.83 (br. s, 1 H, NH), 8.59 (d, *J* = 9.2 Hz, 1 H, 1-H), 8.48 (d, *J* = 7.6 Hz, 1 H, 11-H), 8.11 (d, *J* = 2.6 Hz, 1 H, 4-H), 8.03 (dd, *J* = 9.2, 2.6 Hz, 1 H, 2-H), 7.93 (d, *J* = 7.6 Hz, 1 H, 8-H), 7.57 (dd, *J* = 7.6, 7.6 Hz, 1 H, 10-H), 7.55 (s, 1 H, 7-H), 7.42 (dd, *J* = 7.6, 7.6 Hz, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 155.5 (C-6), 142.5 (C-3), 134.0 (C-11a), 129.6 (C-12a), 128.9, 128.8 (C-4a, -7a), 128.3 (C-6a), 126.2 (C-10), 123.4 (C-9), 123.2 (C-8), 118.3 (C-2), 115.9 (C-1), 114.6 (C-11), 111.3 (C-4), 107.6 (C-7) ppm. EI MS: *m/z* (%) = 279 (63) [M$^+$], 249 (19), 233 (26), 221 (20), 205 (33), 192 (8), 178 (16), 177 (15), 151 (13), 127 (7), 115 (10), 101 (9), 89 (27), 45 (100). $C_{15}H_9N_3O_3$ (279.25): calcd. C 64.52, H 3.25, N 15.05; found C 64.41, H 3.35, N 14.97.

5*H*-Indolo[1,2-*a*]quinoxalin-6-one (57): Yield: 113 mg (94%) (with FeCl$_3$), 110 mg (92%) (with MnO$_2$); m.p. 328−331 °C (decomp., acetic acid), ref.[31] m.p. > 300 °C. IR and ^{1}H NMR spectra are in agreement with those reported[31] in the literature. ^{13}C NMR ([D$_6$]DMSO): δ = 155.7 (C-6), 133.8 (C-11a), 128.6 (C-6a), 128.4 (C-7a), 128.1 (C-4a), 125.4 (C-10), 124.9 (C-12a), 124.4 (C-3), 123.1 (C-2), 122.8 (C-8), 122.3 (C-9), 116.7 (C-4), 115.5 (C-1), 114.5 (C-11), 105.4 (C-7) ppm. EI MS: *m/z* (%) = 234 (100) [M$^+$], 205 (26), 178 (5), 151 (5), 117 (5), 103 (10), 89 (9).

Dehydrogenation of Quinoxalinone 44 to Betaine 58: A solution of iron(III) chloride hexahydrate (3.0 g, excess) in water (6 mL) was filtered to remove some turbidity and added to another of quinoxalinone **44** (0.75 g, 3.0 mmol) in 1,4-dioxane (40 mL). The mixture was stood for 48 h and then the crystals of betaine **58** were collected by filtration, washed with dioxane (3 × 5 mL), and dried under vacuum over phosphorus(V) oxide.

Isoquinolino[2,3-*a*]quinoxalin-13-ium-6-olate (58): Yield: 0.58 g (66%); crystals (water) of compound **58** become dark from ca. 300 °C, but at 360 °C neither melting nor loss of birefringence was detected. IR (nujol): $\tilde{\nu}$ = 1691 (CO) cm^{-1}. ^{1}H NMR (D$_2$O): δ = 10.73 (s, 1 H, 12-H), 9.42 (s, 1 H, 7-H), 8.65 (d, *J* = 7.8 Hz, 1 H, 11-H), 8.52 (d, *J* = 8.0 Hz, 1 H, 1-H), 8.46 (d, *J* = 7.8 Hz, 1 H, 8-H), 8.35 (dd, *J* = 7.8, 7.8 Hz, 1 H, 9-H), 8.22 (dd, *J* = 7.8, 7.8 Hz, 1 H, 10-H), 7.72 (dd, *J* = 8.0, 8.0 Hz, 1 H, 3-H), 7.55 (dd, *J* = 8.0, 8.0 Hz, 1 H, 2-H), 7.43 (d, *J* = 8.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR (D$_2$O): δ = 156.3 (C-6), 142.2 (C-12), 139.3 (C-9), 137.2 (C-7a), 134.8 (C-10), 133.5 (C-3), 131.5 (C-11), 131.1 (C-6a), 130.2 (C-4a), 129.3 (C-8), 128.9 (C-11a), 128.8 (C-7), 126.4 (C-2), 123.1 (C-13a), 119.1 (C-4), 118.3 (C-1) ppm. EI MS: *m/z* (%) = 247 (100) [M$^+$ +1], 218 (17), 190 (3), 128 (6), 124 (5), 109 (4), 102 (4), 89 (3). $C_{16}H_{10}N_2O{\cdot}2.5H_2O$ (291.3): calcd. C 65.97, H 5.19, N 9.62; found C 66.24, H 5.14, N 9.70.

Decarboxylation/Dehydrogenation of 1-Arylindoline-2-carboxylic Acids 11 and 19 to 1-Arylindoles 50 and 51: Manganese(IV) oxide (3.0 g, excess) was added to a stirred solution of the corresponding acid (**11** or **19**) (1.0 mmol) in dichloromethane (50 mL) and after 30 min the inorganic material was filtered off. In the case of 2,4-dinitrophenyl derivative **11**, the solution obtained was evaporated to dryness affording the *N*-substituted indole **50**. In the case of 2-nitrophenyl derivative **19**, after evaporation of solvent, the obtained crude product was percolated through a short silica gel column using chloroform as eluent to remove some tars. Evaporation of the corresponding fractions yielded compound **51**. Both 1-arylindoles were oils that solidified on standing.

1-(2,4-Dinitrophenyl)indole (50): Yield: 0.24 g (85%); m.p. 102−103 °C (carbon tetrachloride/hexane). ^{1}H NMR ([D$_6$]DMSO): δ = 8.97 (d, *J* = 2.6 Hz, 1 H, 3′-H), 8.68 (dd, *J* = 8.8, 2.6 Hz, 1 H, 5′-H), 8.09 (d, *J* = 8.8 Hz, 1 H, 6′-H), 7.68 (m, 1 H, 4-H), 7.58 (d, *J* = 3.4 Hz, 1 H, 2-H), 7.21 (m, 3 H, 5-, 6-, 7-H), 6.82 (d, *J* = 3.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 145.5 (C-4′), 144.4 (C-2′), 136.8 (C-1′), 135.5 (C-7a), 130.6 (C-6′), 129.1 (C-3a), 128.9 (C-5′), 128.6 (C-2), 123.2 (C-6), 121.9 (C-3′), 121.5 (C-5), 121.3 (C-4), 109.5 (C-7), 106.2 (C-3) ppm. EI MS: *m/z* (%) = 283 (100) [M$^+$], 266 (8), 254 (6), 238 (89), 220 (13), 207 (18), 190 (73), 179 (52), 178 (51), 163 (41), 152 (12), 140 (8), 128 (4), 114 (5), 102 (4), 89 (13). $C_{14}H_9N_3O_4$ (283.2): calcd. C 59.37, H 3.20, N 14.84; found C 59.59, H 3.20, N 14.89.

1-(2-Nitrophenyl)indole (51): Yield: 0.19 g (80%); m.p. 81−82 °C (carbon tetrachloride/hexane), ref.[20,37] m.p. 82−83 °C.

Preparation of 1-(4-Acetamido-2-nitrophenyl)indole (52): In the reduction/cyclization of DNP derivative of indoline-2-carboxylic acid (**11**) following Method b, after separation of crude quinoxalinone

37, the filtrate was allowed to stand for 48 h and the precipitated compound, collected by filtration, was 1-(4-amino-2-nitrophenyl)indoline-2-carboxylic acid (**53**). Yield: 2.24 g (75%). ^{1}H NMR ([D$_6$]DMSO): δ = 7.34 (d, J = 8.8 Hz, 1 H, 4-H), 7.10−6.50 (m, 5 H, 5-, 6-, 3′-, 5′-, 6′-H), 5.94 (d, J = 7.7 Hz, 1 H, 7-H), 4.44 (dd, J = 10.9, 7.6 Hz, 1 H, 2-H), 3.36 (dd, J = (−)15.9, 10.9 Hz, 1 H, 3-H$_A$), 3.01 (dd, J = (−)15.9, 7.6 Hz, 1 H, 3-H$_B$) ppm. ES (+) MS: m/z (%) = 643 (11), 621 (64) $[2M + Na]^+$, 322 (20) $[M + Na]^+$, 300 (100) $[M + H]^+$, 238 (8), 187 (14), 105 (31).

Compound **53** is rather sensitive and could not be purified; it decomposes on chromatographic supports and could not be recrystallized. For characterization it was transformed as follows into the *N*-substituted indole **52**: Acetic anhydride (10 mL, excess) was added to a solution of the crude compound **53** in pyridine (100 mL). After 1 h, manganese(IV) oxide (10 g, excess) was added and the mixture was stirred for 2 h. The inorganic material was filtered off and the solution was evaporated to dryness. 5% Hydrochloric acid (100 mL) and chloroform (100 mL) were added to the residue and the mixture was stirred for 10 min. The organic layer was separated, dried with magnesium sulfate, and the solvent was evaporated to dryness. Compound **52** was the major compound of the residue and was isolated by column chromatography on silica gel using a chloroform/methanol (40:1) mixture. Yield: 1.21 g (55% from compound **53**); m.p. 193−195 °C (ethanol). IR (nujol): $\tilde{\nu}$ = 3314 (NH), 1672 (CO) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 10.55 (s, 1 H, NH), 8.48 (d, J = 2.4 Hz, 1 H, 3′-H), 7.92 (dd, J = 8.8, 2.4 Hz, 1 H, 5′-H), 7.65 (d, J = 8.8 Hz, 1 H, 6′-H), 7.60 (m, 1 H, 4-H), 7.42 (d, J = 3.2 Hz, 1 H, 2-H), 7.09 (m, 2 H, 5-, 6-H), 7.01 (m, 1 H, 7-H), 6.65 (d, J = 3.2 Hz, 1 H, 3-H), 2.10 (s, 3 H, CH$_3$) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 169.3 (CO), 145.6 (C-2′), 139.7 (C-4′), 136.4 (C-7a), 130.6 (C-6′), 129.2 (C-2), 128.4 (C-3a), 126.1 (C-1′), 123.9 (C-5′), 122.5 (C-6), 120.9 (C-4), 120.4 (C-5), 114.8 (C-3′), 109.4 (C-7), 103.9 (C-3), 24.1 (CH$_3$) ppm. EI MS: m/z (%) = 295 (100) $[M^+]$, 278 (8), 265 (6), 250 (46), 236 (9), 223 (13), 206 (45), 195 (48), 178 (34), 167 (14), 152 (10), 151 (10), 140 (4), 127 (5), 116 (5), 89 (13). $C_{16}H_{13}N_3O_3$ (295.3): calcd. C 65.08, H 4.44, N 14.23; found C 65.30, H 4.60, N 14.50.

Analysis of Chiral Purity of L-Proline Derivatives by ^{1}H NMR Spectroscopy: This study was carried out by using the chiral shift reagent, europium(III) tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] [(+)-Eu(hfc)$_3$]. Preliminary experiments showed that, in most cases, good separation of enantiomers was achieved using 80−100 mM solutions of the products (P) in CDCl$_3$ and molar ratios [Eu(hfc)$_3$]/[P] = 0.3−0.4. Thus, quinoxalinones **40**, **41**, and **42** (NH), *N*-methylquinoxalinones **46**, **47**, and **48** (N−CH$_3$) and *N*-methoxyquinoxalinones **30** and **31** (N−OCH$_3$) were studied using the conditions described above; DNP- and NP derivatives of L-proline (**8**, **16**), DL-proline (**9**, **17**), and DL-pipecolic acid (**10**, **18**) were studied as the corresponding methyl esters (CH$_3$). In all cases, integration of appropriate signals (in brackets) corresponding to each enantiomer was used to deduce the ratios.

Nitroquinoxalinones **34**−**36** as well as *N*-hydroxyquinoxalinones **27** and **28** are very insoluble in apolar solvents suitable for analysis of enantiomers. In these cases, the enantiomers' ratios were determined indirectly through the study, as commented above, of *N*-methylquinoxalinones **46**−**48** and *N*-methoxyquinoxalinones **30** and **31**, respectively, arising from their methylation.

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