2-[ARYLAMINO(IMINO)]PERHYDROPYRIDO[1,2-*d*][1,3,4]-OXADIAZINE AND 2-[ARYLAMINO(IMINO)]PERHYDRO-PYRROLO[1,2-*d*][1,3,4]OXADIAZINE: HETEROCYCLIC RING SYSTEMS INVOLVING A BRIDGE-HEAD NITROGEN

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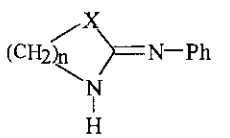
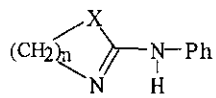
Abstract - Hydrazino alcohols (**1 - 4**) were converted with phenyl or 4-chlorophenyl isothiocyanate into their thiourea derivatives (**5a,b**, **6a,b**, **9a,b** and **10a,b**) which then were cyclized by treatment with methyl iodide and alkali to furnish 2-[arylamino(imino)]perhydropyrido[1,2-*d*]-[1,3,4]oxadiazines (**7a,b**) and perhydropyrrolo[1,2-*d*][1,3,4]oxadiazines (**12a,b**) and their 2-aryl-imino-3*N*-methyl derivatives (**8a,b** and **13b**). The nmr spectra and X-ray crystallographic analysis indicated that the 1,3,4-oxadiazines adopt rigid *cis*- or *trans*-fused ring conformations, depending on the parent ring size and the 3*N*-substituent. It was found that in the unsubstituted 1,3,4-oxadiazines (**7a,b** and **12a,b**) involving a potential tautomeric equilibrium, the amino form is most likely to predominate.

INTRODUCTION

Various cyclic guanidines and their heteroanalogues (**A**, **B**; X = C, N, S or O) have been reported. Besides their syntheses and biological activities,[1a,b] the difficulties involved in the unambiguous determination of the predominant tautomeric form, either the imino form **A** with an *exo* C=N or the amino form **B** with an *endo* C=N bond, have attracted attention.[2] The latest reports indicate that there is in fact a rapid interconversion between the tautomers and in most cases the imino form predominates.

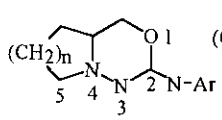


A, imino form

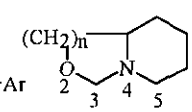


B, amino form

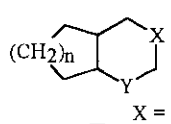
This paper describes the synthesis and structure determination (conformation and prototropic tautomerism) of a compound of type **C** (n = 1, 2), containing a bridged nitrogen and a 1,3,4 arrangement of heteroatoms. Each of the 1,3,4-oxadiazines reported here appears to be conformationally homogeneous, adopting solely the *trans* or the *cis*-fused conformation. This is rather unex-



C



D

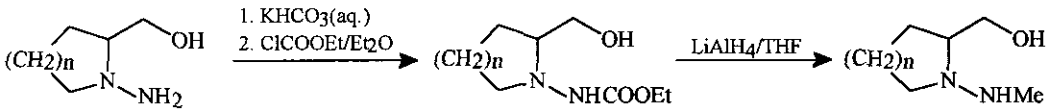


E X = O, N, S; Y = O, N

pected considering the conformational behaviour of related 5/6 and 6/6-fused compounds containing a 1,3 arrangement of heteroatoms as in **D**[3] and **E**[4] which earlier has been extensively studied.

SYNTHESIS

Hydrazino alcohols (**1**) and (**2**) were prepared, in good yields, from *S*-proline and (±)-2-hydroxymethyl-piperidine, respectively.[5] Following earlier reported methods,[6] the *N*-methyl-substituted hydrazino alcohols (**3**) and (**4**) (Scheme 1) were prepared from the corresponding unsubstituted hydrazino alcohols (**1**) and (**2**) by treatment with ethyl chloroformate, followed by reduction with $LiAlH_4$. The piperidine-carbamate derivative of **2** was much more difficult to reduce than the carbamate prepared from **1**. Whereas the latter was reduced in 18 h with a yield of 76%, the former required a 72 h refluxing to achieve a yield of 40%. The hydrazino alcohols were oily products and were purified either by distillation *in vacuo* or by column chromatography. They were air-sensitive and decomposed to some extent during the purification procedures and storage (at -23 °C).

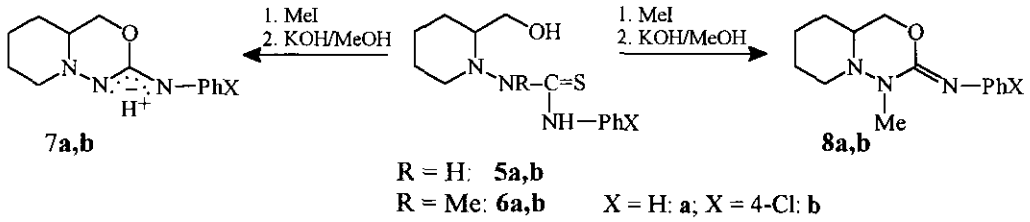


n = 1: **1**
n = 2: **2**

n = 1: **3**
n = 2: **4**

Scheme 1

Hydrazino alcohols (**1- 4**) were transformed to the corresponding thiourea derivatives (**5a,b**, **6a,b**, **9a,b** and **10a,b**) in good yields (65-80%) by treatment with phenyl or 4-chlorophenyl isothiocyanate. A variety of cyclization methods of such thiourea derivatives into 2-imino-substituted ring systems have been reported.[7] Depending on the method chosen, the end-product contains either an oxygen or a sulfur atom in the hetero ring. The best way to obtain the oxygen analogues is by reacting the thiourea derivatives with methyl iodide, to yield the corresponding thiouronium salts, which are then treated with an alkali to induce nucleophilic attack by oxygen on the positive carbon atom of the salt, a mechanism suggested by Ignatova *et al.*[8] This method, applied to **5a,b** and **6a,b**, afforded the 1,3,4-oxadiazines (**7a,b**) and (**8a,b**) in fairly good yields (Scheme 2). The stereochemistry of the decalin-related ring systems was established by means of nmr spectroscopic and X-ray diffraction analysis. The unsubstituted **7a,b** adopted exclusively a *trans*-fused conformation, as expected, on the basis of the results of earlier work,[5, 9] but the 3*N*-methyl-substituted **8a,b** surprisingly adopted a stereohomogeneous *cis N-out* conformation.

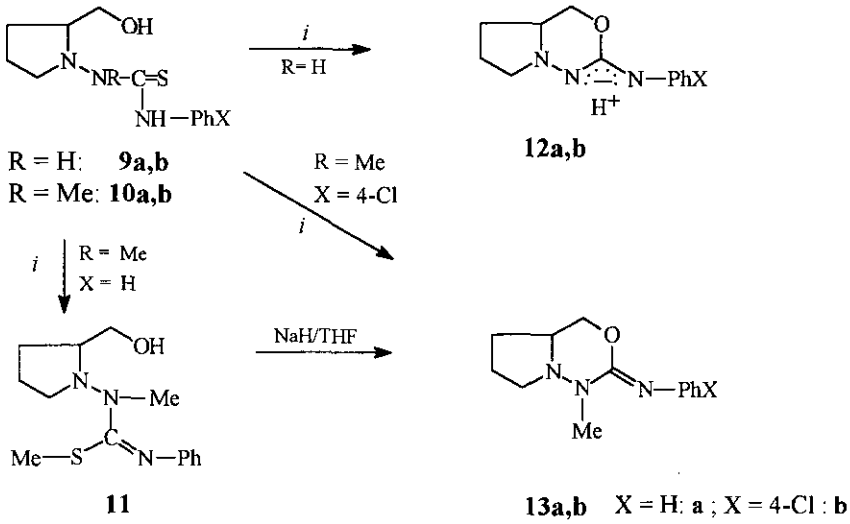


7a,b 8a,b

R = H: **5a,b**
R = Me: **6a,b** X = H: **a**; X = 4-Cl: **b**

Scheme 2

The unsubstituted pyrrolothiourea derivatives (**9a,b**) (Scheme 3) underwent cyclization as readily as the thiourea derivatives (**5a,b**-**6a,b**) whereas the *N*-methyl-substituted pyrrolothioureas (**10a,b**) displayed a considerable difference in cyclization reactivity. The ring closure of **10b** yielded **13b** in very poor yield; for **10a**, no ring-closed product could be isolated, but instead the isothiouronium derivative (**11**) was obtained. Fülöp *et al.* reported similar behaviour for related *cis* thiourea derivatives with cyclopentane and cyclohexane skeletons.[1a] They were unsuccessful in transforming the isothiouronium derivatives to the corresponding 1,3-oxazines by heating with alkali or treatment with mercury(II) chloride or lead(II) nitrate. However, we were able to cyclize **11** quantitatively to the corresponding oxadiazine (**13a**) by using sodium hydride. The stereochemistry of the perhydropyrrolooxadiazines (**12a,b**) and (**13a,b**) is not as clear as in the case of the pyrido-oxadiazines. The unsubstituted **12a,b** adopt a *cis*-fused conformation having the C7a-C8 bond in an *axial* orientation, while the 3*N*-Me derivatives (**13a,b**) also adopted a *cis*-fused conformation, though having the C7a-C8 bond in an *equatorial* orientation.



12a,b

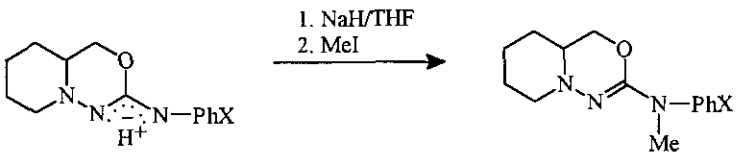
11 13a,b X = H: **a** ; X = 4-Cl : **b**

i, MeI/MeOH, 15% methanolic KOH

Scheme 3

Efforts to prepare the corresponding sulfur analogues, i.e. the thiadiazines, by treating the thiourea derivatives with thionyl chloride or ethanolic hydrogen chloride in different concentrations, gave very heterogeneous products and no attempts at isolation were therefore made.

The reactions of potentially tautomeric, cyclic amidine systems, with isocyanates, have been found to occur exclusively at the *endo* nitrogen, and the carbamoyl group then migrates intramolecularly to the *exo* nitrogen.[10] When the potentially tautomeric **7a,b** were treated with sodium hydride, followed by methyl iodide, only the *exo* methylated **14a,b** were formed (~60%) (Scheme 4).



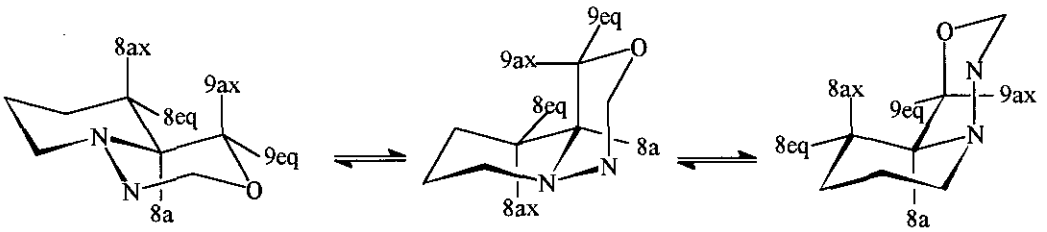
7a,b X = H: **a** ; X = 4-Cl: **b** **14a,b**

Scheme 4

STRUCTURE DETERMINATION

NMR spectroscopy. The structures of **7a,b**, **8a,b** and **12a,b-14a,b** were established by means of ^{1}H and ^{13}C NMR studies. The spectral data and calculated couplings constants[11] are given in Tables 1-6. The unequivocal assignments of the spectra were achieved through the concerted use of 2D (^{13}C-^{1}H) heterocorrelation, 2D ^{1}H-^{1}H COSY and 2D NOESY nmr experiments.

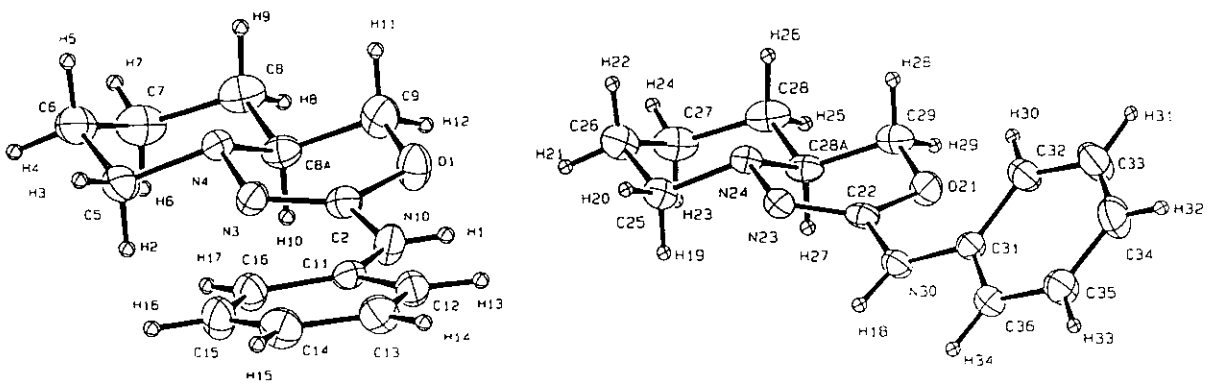
Solutions of these compounds involve a conformational equilibrium between a rigid *trans*-fused conformer (**A**) (Figure 1) and two *cis*-fused conformers, the *N-out* (**B**) and the *N-in* (**C**) forms, which are interconvertible as a consequence of nitrogen inversion and ring inversion processes.



trans (**A**) *cis N-out* (**B**) *cis N-in* (**C**)

Figure 1

Perhydropyrido[1,2-*d*][1,3,4]oxadiazines (7a,b). The unsubstituted, potentially tautomeric, 1,3,4-oxadiazines (**7a,b**) were found to exist in a *trans*-annellated conformation (**A**) (H-8a located *trans* with respect to the lone pair of the bridged nitrogen). This was proved by the ^{3}J couplings from H-8a to the methylene protons at C-8 and C-9 (Table 2). The measured $^3J(8a,9eq)$ = 3.1 Hz and $^3J(8a,9ax)$ = 9.7 Hz support a *trans* and/or a *cis N-out* conformation. The magnitude of the observed $^3J(8a,8ax)$(= 11.5 Hz) clearly proves that **7a,b** exist in a *trans*-fused conformation. The large $\Delta 5eq,5ax$ value of 0.94 ppm for **7a,b** is similar in magnitude to those observed for 2-phenyl-perhydropyrido[1,2-*d*][1,3,4]oxadiazine (100% *trans*) **15** (0.92 ppm)[5] and perhydropyrido[1,2-*c*][1,3]oxazine (98% *trans*, 2% *cis N-in*) **16** (0.76 ppm),[9] and is in accord with **7a,b** adopting exclusively a *trans*-fused conformation. The *trans*-fusion was also confirmed in the solid phase by X-ray analysis, where two the rotamers (**7a**) and (**7a′**) were observed in the same crystal, probably due to packing effects (Figure 2). Selected bond distances and angles for **7a** are presented in Table 8.



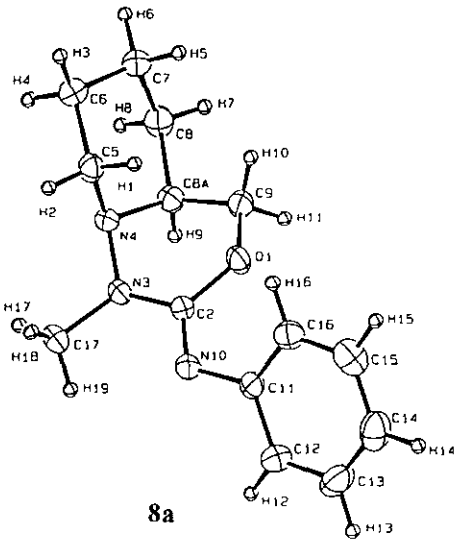
7a **7a′**

Figure 2. ORTEP plot and labelling for **7a** and its rotamer **7a′**.

3*N*-Methylperhydropyrido[1,2-*d*][1,3,4]oxadiazines (8a,b). The 3*N*-methyl-substituted 1,3,4-oxadiazines (**8a,b**) surprisingly adopt a *cis N-out* (**B**) conformation (Figure 1). According to earlier studies on perhydropyrido-1,3-oxazines (**16**), conformation (**B**) is not expected to make any significant contribution to the equilibrium, because of several destabilizing non-bonding interactions relative to conformations (**A**) and (**C**).[3] The existence of stabilizing intramolecular (hydrogen-bond-like) bondings in **8a,b**, favouring conformation (**B**), was excluded by running ^{1}H and ^{13}C NMR experiments in methanol.

The observed values of ^{3}J (8a,9*eq*) = 5.7 Hz, ^{3}J (8a,9*ax*) = 11.7 Hz, ^{3}J (8a,8*eq*) = 2.1 Hz and ^{3}J (8a,8*ax*) = 5.3 Hz exclude the existence of conformations (**A**) and (**C**) in **8a,b**. The substantial downfield shift of H-9ax (+0.43 ppm) in **8a,b** is due to strong steric hindrance between H-9*ax*, H-7*ax* and H-5*ax*, causing an electrostatic repulsion between the protons, which decreases the electron density around H-9ax.[12] This deshielding of H-9*ax* is possible only in the *cis N-out* conformation (**B**). The marked downfield shift of H-8a in **8a,b** (δ 3.66 ppm) as compared with that in **7a,b** (δ 2.45 ppm) is in accordance with H-8a being situated *syn equatorial-axial* with respect to the bridge nitrogen lone pair in **8a,b**.[13] Additionally, the small chemical shift differences Δ5*eq*,5*ax* of 0.24 ppm and 0.26 ppm in **8a,b**, respectively, are consonant with these compounds existing in a *cis*-annellated conformation.[14]

The ^{13}C signals of a *cis*-decalin (*i.e.* 6/6-fused) system are diamagnetically shifted as compared with those of the corresponding *trans*-decalin, as a consequence of a steric compression shift.[12] This was observed in a comparison of the carbon chemical shifts of **7a,b** and **8a,b** (Table 3). A substantial shielding and an upfield shift were observed especially for the C-9, C-8a, C-7 and C-5 signals in **8a,b**. The ^{13}C chemical shift differences in *trans*-fused **7a,b** and cis-fused **8a,b** are in good agreement with the results of Crabb *et al.*[9] (Table 3). Conformation (**B**) in the solid phase for **8a** was confirmed by X-ray analysis (Figure 3). Selected bond distances and angles for **8a** are presented in Table 9.



8a

Figure 3. ORTEP plot and labelling of **8a**.

2-(*N*-Methyl-*N*-phenylamino)perhydropyrido[1,2-*d*][1,3,4]oxadiazine (14a,b). The methylated (**14a,b**) were unambiguously established as *trans*-annellated conformers, having nmr spectral data almost identical with those of **7a,b** (Table 1). The *exo*-methylation was confirmed by means of 2D NOESY experiments, where an interaction was observed between the -*N*Me and *ortho*-H signals and the H-9*ax* signal.

Table 1. Selected ^{1}H NMR chemical shifts for **7a,b-8a,b**[a], **14a,b** and **15**[b] at 294 K

compd	*c/t*	H-9*eq*	H-9*ax*	H-8a	H-5*eq*	H-5*ax*	Δ5*eq*,5*ax*	*o*-H	*m*-H	*p*-H
7a	*trans*	4.18	4.10	2.45	3.39	2.45	0.94	7.28	7.22	6.90
7b	*trans*	4.17	4.09	2.43	3.38	2.45	0.93	7.17	7.25	-
8a	*cis*	4.03	4.53	3.67	3.09	2.85	0.24	6.96	7.23	6.93
8b	*cis*	4.04	4.53	3.65	3.09	2.83	0.26	6.90	7.16	-
14a	*trans*	4.10	4.03	2.44	3.39	2.45	0.94	7.28	7.10	7.04
14b	*trans*	4.04	3.96	2.37	3.30	2.34	0.96	6.95	7.15	-
15	*trans*	4.28	4.14	2.58	3.53	2.61	0.92			

[a] For numbering, see molecular structure. [b] Data from ref. 5

Table 2. Proton - proton coupling constants (Hz) for **7a**, **8a** and **15**[a]

compd	*c/t*	^{2}J(9*eq*, 9*ax*)	^{3}J(9*eq*, 8a)	^{3}J(9*ax*, 8a)	^{3}J(8a, 8*eq*)	^{3}J(8a, 8*ax*)	^{2}J(5*eq*, 5*ax*)
7a	*trans*	-9.9	3.1	9.7	2.7	11.5	-11.4
8a	*cis*	-10.9	5.7	11.7	2.1	5.3	-10.9
15	*trans*	-10.3	3.1	9.0	3.2	11.3	-11.3

[a] Data from ref. 5

Table 3. Selected ^{13}C NMR chemical shifts for **7a,b-8a,b**, **14a,b**, **15** and **16** (294 K) compared with the ^{13}C chemical shifts for *trans* (**16-t**) and *cis* (**16-c**) perhydropyrido[1,2-*d*][1,3]oxazine separated and measured at 203 K

compd	*c/t*	C-9	C-8a	C-5	C-7	Me	C-2	(s) C	(o) C	(m) C	(p) C
7a	*trans*	70.7	56.0	57.0	23.5	-	143.2	140.1	117.6	128.9	121.1
7b	*trans*	70.7	55.9	57.0	23.5	-	142.9	138.7	118.7	128.7	125.5
8a	*cis*	65.3	47.1	52.4	18.4	37.5	148.1	148.1	123.6	128.5	121.6
8b	*cis*	65.1	47.1	52.2	18.2	37.4	148.2	146.7	124.8	128.3	126.3
14a	*trans*	70.4	55.8	56.8	23.4	38.6	146.9	145.5	123.0	128.7	123.3
14b	*trans*	70.6	55.7	56.8	23.4	38.8	146.3	144.1	123.7	128.6	128.4
15[a]	*trans*	69.6	54.6	56.1	23.5	-	-	-	-	-	-
16-*t*[b]	*trans*	32.5	60.8	49.1	24.0	-	-	-	-	-	-
16-*c*[b]	*cis*	24.0	53.4	44.6	18.7						

[a] Data from ref. 5, [b] Data from ref. 9

The three-component equilibria shown in Figure 1 can, in principle, also be applied to the pyrrolo[1,3,4]-oxadiazines (**12a,b**) and (**13a,b**). However, the ring-fusion strain, due to the 5/6-fusion, flattens the bridge nitrogen bonds, forcing the N(4)-N(3) bond, in both *cis* conformers, to adopt a *pseudo-equatorial* orien-

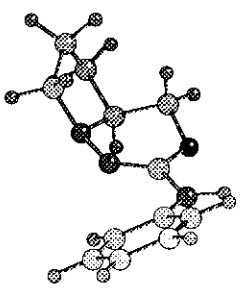
tation. This flattening is enhanced by the unsaturated moiety in the oxadiazine ring. Consequently, the two *cis* conformers (**B** and **C**) differ mainly in the orientation of the C(7a)-C(8) bond (*axial* or *equatorial*).

Perhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (12a,b). The couplings constants $^3J(7a,8eq)$ = 3.6 Hz and $^3J(7a,8ax)$ = 9.0 Hz, of the ABX spin system in **12a,b** (Table 5) are in accord with these compounds assuming either a *trans* (**A**) or a *cis* (**B**) conformation. The small chemical shift differences, $\Delta 5eq,5ax$, of 0.05 ppm and 0.04 ppm in **12a,b** respectively, are reported as typical values for a 100% *cis*-fused conformation.[5, 14] Further evidence for **12a,b** adopting the *cis* (**B**) conformation was the fact that their nmr data were almost identical with those of an earlier compound we reported, perhydropyrrolo[1,3,4]-oxadiazine (**17**)[5] (Tables 4-6), where the stereochemistry was demonstrated by X-ray analysis to be *cis* (**B**).

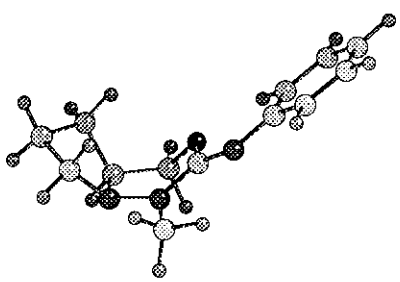
3*N*-Methylperhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (13a,b). The stereostructure of **13a,b** was confirmed as *cis* (**C**) by the small coupling constants, $^3J(7a,8eq)$ = 3.1 Hz and $^3J(7a,8ax)$ = 4.7 Hz and the downfield shifts of H-7a (+0.72 ppm and +0.65 ppm) as compared with those for **12a,b**. The small ^3J values, together with the fact that the ^{13}C NMR spectrum for **13b** did not change even at 178 K strongly suggest that **13a,b** exist in a stereohomogeneous system.

The downfield ^{13}C-chemical shifts of C-7 and C-7a (+2-3 ppm) for **13a,b** as compared with those for **12a,b**, together with the large $\Delta 5eq,5ax$ values, indicates a *trans*/*cis* equilibrium[13,14] in **13a,b**. However, as mentioned above, we rather assume these spectral differences to originate from **12a,b** adopting the *cis* conformation (**B**), whereas **13a,b** adopt the *cis* conformation (**C**).

The COSMIC force field energy-minimized representations of **12a** and **13a**, as generated by the NEMESIS program,[15] are shown in Figure 4, where the flattening of the bridged nitrogen bonds is evident, forcing the N(3)-N(4) bond into an *pseudo-equatorial* position.



12a



13a

Figure 4

Table 4. Selected ^{1}H NMR chemical shifts for **12a,b**, **13a,b** and **17**[a]

compd	H-8*eq*	H-8*ax*	H-7a	H'-5	H''-5	Δ5',5''	*N*-R	*p*-H	*m*-H	*o*-H
12a	4.38	3.98	~3.07	3.04	2.99	0.05	5.71	6.91	7.20-7.28	
12b	4.39	3.97	~3.07	~3.04	~3.00	0.04	5.67	-	7.16-7.26	
13a	4.13	3.93	3.79	3.39	2.71	0.68	3.13	6.95	7.25	6.95
13b	4.03	3.87	3.72	3.33	2.62	0.71	3.03	-	7.16	6.90
17	4.52	3.82	3.15	3.29	3.27	0.02				

[a] Data from ref. 5

Table 5. Proton - proton coupling constants (Hz) for **12a**, **13a** and **17**[a]

compd	^{2}J(8',8'')	^{3}J(8',7a)	^{3}J(8'',7a)	^{3}J(7a,7')	^{3}J(7a,7'')	^{2}J(5',5'')
12a	-9.8	3.6	9.0	7.4	8.4	-9.5
13a	-10.9	3.1	4.7	7.7	6.7	-8.6
17	-9.9	3.9	8.9	7.2	9.7	-9.2

[a] Data from ref. 5

Table 6. Selected ^{13}C NMR chemical shifts for **12a,b**, **13a,b** and **17**[a]

compd	C-5	C-6	C-7	C-7a	C-8	*N*-Me	C-2	(s) C	(o) C	(m) C	(p) C
12a	55.5	21.3	25.2	55.5	68.6	-	144.9	140.1	117.7	129.0	121.3
12b	55.5	21.3	25.2	55.5	68.8	-	144.6	138.6	118.8	128.9	126.0
13a	52.0	22.0	28.2	57.8	68.0	37.7	153.4	146.7	123.3	128.5	122.4
13b	52.1	21.9	28.0	57.7	68.0	37.6	153.3	145.8	124.5	128.5	127.2
17	54.3	21.6	26.5	55.4	68.5						

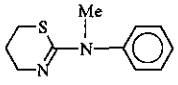
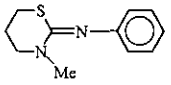
[a] Data from ref. 5

Prototropic tautomerism? The literature states that one can unambiguously determine the predominant tautomer (imino or amino) in aryl cyclic amidines *via* the significantly different electron distribution in the aromatic region.[16] The potentially tautomeric structures (**7a,b**) and (**12a,b**) (hereinafter = unsubstituted) exhibited remarkable similarity as conserns the ^{1}H and ^{13}C chemical shifts of the aryl group (Tables 1, 3, 4 and 6). A similar homogeneity of the chemical shifts was found for **8a,b** and **13a,b**, which have a fixed imino structure, due to their 3*N*-methyl substituent.

The presence of a NOE interaction between the *N*-H and the *ortho*-H in **7a**, and the fact that the alkylation of **7a,b** yielded exclusively the *exo*-nitrogen methylated compounds (**14a,b**), support the existence of an amino tautomer in **7a,b** and **12a,b**. Additionally X-ray analysis shows an amino structure in the solid state for **7a**. We suggest, therefore, that the position of the tautomeric equilibrium is biased towards the amino form in the unsubstituted compounds.

The resonance differences in the ^{13}C signals of the aromatic region, observed between those for the unsubstituted and the imino compounds (Table 7), is not in accord with the general method given for an unambiguous determination and distinction of amino and imino tautomers. The upfield shifts of the C-2 and *ipso*-C signals for the unsubstituted compounds, suggesting an amino structure, are in agreement with the results of Jackman *et al.*,[16] but the reported strong deshielding and lowfield shifts of the *ortho* and *para*-carbon signals for the amino tautomers could not be observed in our case. In contrast, we found that the *ortho*-carbon signals of the unsubstituted compounds displayed an upfield shift (-7 ppm), whereas the *para*-carbons had the same resonance shift in the unsubstituted and the imino compounds. The ^{13}C chemical shifts obtained for the aromatic ring in the fixed amino structures (**14a,b**) showed no correlation with those of the unsubstituted and the imino analogues, making it impossible for us to use the resonances of the aromatic region to determine the predominant tautomeric structure in the present compounds.

Table 7. Selected ^{13}C NMR chemical shifts for 2-aminothiazines[16] and **7a**, **8a** and **14a**

	ipso	*ortho*	*meta*	*para*	c-2
	145.1	128.8	128.3	126.5	150.6
	150.0	122.8	128.5	122.5	152.3
7a	140.1	117.6	128.9	121.1	143.2
8a	148.0	123.6	128.5	121.6	148.1
14a	145.5	123.0	128.7	123.3	146.9

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Nmr spectra were recorded on JEOL JNM-L-400 and JNM-A-500 instruments. The chemical shifts (δ), given in ppm, are referred to tetramethylsilane. $CDCl_3$ was used as solvent. The couplings constants given for **7a**, **8a**, **12a** and **13a** are calculated by the iterative Perch program.[11] The elemental analyses were performed on a Perkin Elmer Analyser 2400 C, H, N, S / O and the high-resolution mass spectra were obtained on a VG-7070E spectrometer.

Compounds (**1**) and (**2**) were prepared according to a method reported earlier.[6]

1-Methylamino-2-hydroxymethylpyrrolidine (3). Hydrazino alcohol (**1**) (3.95 g, 34 mmol) was dissolved in 30 mL of ether and $NaHCO_3$ (4.60 g, 55 mmol) in 20 mL of water was added. Ethyl chloroformate

(3.54 mL, 37 mmol) was added dropwise through a dropping funnel. The mixture was stirred overnight and the organic phase was separated. The aqueous phase was further extracted with ethyl acetate (3 x 50 mL) and the combined organic phase was dried over Na_2SO_4 and evaporated to obtain the crude carbamate derivative (3.1 g, 49%), which was used without further purification (recrystallized from benzene, mp 95-98 °C). The carbamate (3.0 g, 16 mmol) was treated with a suspension of $LiAlH_4$ (2.4 g, 64 mmol) in 80 mL of dry THF at 70 °C (oil bath) for 18 h. The excess of $LiAlH_4$ was carefully decomposed by adding 4.5 mL of aqueous 10% potassium hydroxide to the ice-cold reaction mixture, which, after the addition, was refluxed for 20 min. The precipitate formed was filtered off under suction and washed several times with small amounts of hot THF. The filtrate was dried over Na_2SO_4 and the solvent was evaporated (water bath T = 30 °C). The oily residue was column chromatographed (silica gel, toluene - methanol 90:10 as eluent), to afford a slightly yellow oil, **3** (1.6 g, 76%). ^{1}H NMR δ: 3.71 (dd, 1H, J = 2.7 and 10.5 Hz), 3.62 (dd, 1H, J = 8.2 and 10.5 Hz), 3.55 (m, 1H), 2.66-2.58 (m, 5H), 2.08 (m,1H), 2.00-1.70 (m, 3H), 1.35-1.15 (m, 2H). ^{13}C NMR δ: 67.3, 65.1, 55.7, 36.5, 24.2, 20.7.

1-Methylamino-2-hydroxymethylpiperidine (4). Compound (**4**), was prepared from 1-amino-2-hydroxymethylpiperidine (**2**) in the same manner as described above (68%, mp 83-85 °C). The reduction of the carbamate required a substantially longer time (to 72 h). The hydrazino alcohol (**4**) was obtained as an oil, in 40% yield, calculated on the carbamate. ^{1}H NMR δ: 3.68 (m, 1H), 3.46 (m, 1H), 3.34 (m, 1H), 2.58 (br s, 3H), 2.30 (m, 1H), 1.95 (m, 1H), 1.71-1.63 (m, 4H), 1.54-1.43 (m, 2H), 1.27-1.05 (m, 2H). ^{13}C NMR δ: 69.7, 65.5, 62.7, 35.5, 28.4, 25.3, 23.5.

General procedure for the preparation of isothiourea derivatives (5a,b-6a,b and 9a,b-10a,b.) Hydrazino alcohol (**1-4**) (10 mmol) was dissolved in 20 mL of dry ether, and (11 mmol) phenyl or 4-chlorophenyl isothiocyanate was added. A crystalline product soon separated out from the solution and was filtered off. All the products were used without further purification. Melting points and yields were as follows; **5a**: 141-143 °C, 68%; **5b**: 156-157 °C, 76%; **6a**: 122-123 °C, 70%; **6b**: 116-118 °C, 47%; **9a**: 143-146 °C, 30%: **9b**; 157-160 °C, 39%; **10a**: oil, no purification; **10b**: oil, no purification.

General procedure for the cyclization of thioureas 5-6 a,b and 9-10 a,b by treatment with MeI and alkali. Thiourea derivative (**5a,b**, **6a,b**, **9a,b** or **10a,b**, (2 mmol)) was dissolved in 5-10 mL of dry methanol and 2.5 mL (40 mmol) of methyl iodide was then added. After stirring for 5-6 h at rt, the methanol and excess methyl iodide were evaporated off. The residue was dissolved in 25 mL of 15% methanolic potassium hydroxide and the solution was stirred at rt overnight. The solvent was removed and 25 mL of ice-cold water was added to the residue, followed by extraction with chloroform (3 x 40 mL). The organic phase was dried over Na_2SO_4 and the solvent was evaporated. Recrystallization furnished the pure ring-closed products in fairly good yields, with the exceptions of **10a,b**. An oily product was obtained in very poor yield with **10b**, and starting from **10a** no ring-closed product was isolated in the reaction, but instead the isothiouronium derivative (**11**), which was purified by column chromatography (silica gel; petroleum ether - ethyl acetate 65:35 as eluent) in 65% yield.

2-Phenylaminoperhydropyrido[1,2-*d*][1,3,4]oxadiazine (7a). Recrystallized from n-hexane, 64%, mp 70-72 °C. ^{1}H NMR δ: 7.28 (m, 2H, *ortho*-H), 7.22 (m, 2H, *meta*-H), 6.90 (m, 1H, *para*-H), 5.57 (br s, N-H), 4.18 (dd, J = 3.1 and 9.9 Hz, H-9eq), 4.10 (dd, J = 9.7 and 9.9 Hz, H-9ax), 3.39 (m, J = 1.5, 2.7, 4.1 and 11.4 Hz, H-5eq), 2.39 (m, J = 2.7, 11.4 and 12.6 Hz, H-5ax), 2.36 (m, J = 2.7, 3.1, 9.7 and 11.5 Hz, H-8a), 1.74 (m, J = 1.5, 2.6, 3.3, 4.1, 4.6 and 13.4 Hz, H-7eq), 1.67 (m, J = 2.3, 2.7, 2.7, 4.2, 4.6 and 12.7 Hz, H-6eq), 1.64 (m, J = 3.3, 4.1, 12.6, 12.6 and 13.5 Hz, H-6ax), 1.58 (m, J = 2.3, 2.6, 2.7, 3.9 and 13.0 Hz, H-8eq), 1.28 (m, J = 3.9, 4.2, 13.3, 13.4 and 13.5 Hz, H-7ax), 1.17 (m, J = 4.1, 11.5, 13.0 and

13.3 Hz, H-8ax). ^{13}C NMR δ: 143.2 (C-2), 140.1 (*ipso*-C), 128.9 (*meta*-C), 121.1 (*ortho*-C), 117.6 (*para*-C), 70.7 (C-9), 57.0 (C-5), 56.0 (C-8a), 27.1 (C-8), 25.5 (C-6), 23.5 (C-7). *Anal.* Calcd for $C_{13}H_{17}N_3O$, C 67.51, H 7.41, N 18.17. Found C 67.60, H 7.40, N 17.96.

2-(4-Chlorophenylamino)perhydropyrido[1,2-*d*][1,3,4]oxadiazine (7b). Recrystallized from n-hexane, 57%, mp 100-102 °C. ^{1}H NMR δ: 7.17 (m, 2H, *ortho*-H), 7.25 (m, 2H, *meta*-H), 5.60 (br s, N-H), 4.17 (dd, J = 3.4 and 10.1 Hz, H-9eq), 4.09 (t, J = 9.9 and 9.9 Hz, H-9ax), 3.38 (m, H-5eq), 2.45 (m, H-5ax), 2.43 (m, H-8a), 1.81 (m, H-7eq), 1.78-1.62 (m, 3H, H-6eq, H-6ax, H-8eq), 1.35 (m, H-7ax), 1.23 (m, H-8ax). ^{13}C NMR δ: 142.9 (C-2), 138.7 (*ipso*-C), 128.7 (*meta*-C), 125.8 (*para*-C), 118.7 (*ortho*-C), 70.7 (C-9), 57.0 (C-5), 55.9 (C-8a), 27.0 (C-8), 25.5 (C-6), 23.5 (C-7). HRMS calcd for $C_{13}H_{16}N_3OCl$, 265.0988; found 265.0982.

2-Phenylimino-3*N*-methylperhydropyrido[1,2-*d*][1,3,4]oxadiazine (8a). Recrystallized from n-hexane, 61%, mp 97-99 °C. ^{1}H NMR δ: 7.23 (m, 2H, *meta*-H), 6.96 (m, 2H, *ortho*-H), 6.93 (m, 1H, *para*-H) 4.52 (dd, J = 10.9 and 11.7 Hz, H-9ax), 4.02 (dd, J = 5.7 and 10.9 Hz, H-9eq), 3.66 (m, J = 2.1, 5.3, 5.7 and 11.9 Hz, H-8a), 3.19 (s, 3H, -CH$_3$), 3.08 (m, J = 1.3, 3.0, 4.1 and 10.9 Hz, H-5eq), 2.84 (m, J = 2.7, 10.9 and 12.6 Hz, H-5ax), 1.87 (m, J = 4.7, 5.3, 13.7 and 14.2 Hz, H-8ax). 1.77 (m, J = 2.1, 2.9, 3.0, 3.9 and 13.5 Hz, H-6eq), 1.60 (m, J = 4.0, 4.1, 12.6, 13.2 and 13.5 Hz, H-6ax), 1.55 (m, J = 2.1, 2.1, 2.5, 4.3 and 14.2 Hz, H-8eq), 1.53 (m, J = 1.3, 2.5, 2.9, 4.0, 4.7 and 14.1 Hz, H-7eq), 1.34 (m, J = 3.9, 4.3, 13.2, 13.7 and 14.1 Hz, H-7ax), ^{13}C NMR δ: 148.1 (C-2), 148.0 (*ipso*-C), 128.5 (*meta*-C), 123.6 (*ortho*-C), 121.6 (*para*-C), 65.3 (C-9), 52.4 (C-5), 47.1 (C-8a), 37.5 (-CH$_3$), 25.6 (C-8), 25.1 (C-6), 18.4 (C-7). *Anal.* Calcd for $C_{14}H_{19}N_3O$, C 68.54, H 7.81, N 17.13. Found C 68.30, H 7.86, N 16.91.

2-(4-Chlorophenylimino)-3*N*-methylperhydropyrido[1,2-*d*][1,3,4]oxadiazine (8b). Recrystallized from n-hexane, 60%, mp 94-96 °C. ^{1}H NMR δ: 7.16 (m, 2H, *meta*-H), 6.90 (m, 2H, *ortho*-H), 4.53 (dd, J = 10.9 and 11.9 Hz, H-9ax), 4.03 (dd, J = 5.5 and 10.9 Hz, H-9eq), 3.65 (m, H-8a), 3.18 (s, 3H, -CH$_3$) 3.09 (m, H-5eq), 2.83 (m, H-5ax), 1.85 (m, H-8ax). 1.78 (m, H-6eq), 1.66-1.52 (m, 3H, H-6ax, H-8eq and H-7eq), 1.34 (m, H-7ax), ^{13}C NMR δ: 148.2 (C-2), 146.7 (*ipso*-C), 128.3 (*meta*-C), 126.3 (*para*-C), 124.6 (*ortho*-C), 65.1(C-9), 52.2 (C-5), 47.1 (C-8a), 37.4 (-CH$_3$), 25.4 (C-8), 25.0 (C-6), 18.2 (C-7). *Anal.* Calcd for $C_{14}H_{18}N_3OCl$, C 60.10, H 6.50, N 15.00. Found C 60.28, H 6.43, N 14.81.

2-Phenylaminoperhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (12a). Recrystallized from diisopropyl ether, 47%, mp 148-149 °C. ^{1}H NMR δ: 7.28-7.20 (m, 4H, *ortho*-H and *meta*-H), 6.91 (m, 1H, *para*-H), 5.71 (br s, N-H), 4.31 (dd, J = 3.6 and 9.8 Hz, H-8eq), 3.91 (dd, J = 9.0 and 9.8 Hz, H-8ax), 3.04 (m, J = 6.0, 7.3 and 9.5 Hz, H′-5), 3.00 (m, J = 3.6, 7.4, 8.4 and 9.0 Hz, H-7a), 2.97 (m, J = 5.9, 8.0 and 9.5 Hz, H′′-5), 1.95 (m, J = 3.1, 7.4, 9.6, and 12.7 Hz, H′-7), 1.81(m, J = 3.1, 5.9, 7.3, 10.3 and 12.4 Hz, H′-6), 1.77 (m, J = 6.0, 8.0, 8.1 9.6 and 12.4 Hz, H′′-6), 1.45 (m, J = 8.0, 8.4, 10.3 and 12.7 Hz, H′′-7). ^{13}C NMR δ: 144.9 (C-2), 140.1 (*ipso*-C), 129.0 (*meta*-C), 121.3 (*para*-C), 117.7 (*ortho*-C), 68.6 (C-8),55.4 (C-5), 55.0 (C-7a), 25.2 (C-7), 21.3 (C-6). *Anal.* Calcd for $C_{12}H_{15}N_3O$, C 60.34, H 6.96, N 19.34. Found C 60.31, H 6.89, N 19.04.

2-(4-Chlorophenylamino)perhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (12b). Recrystallized from diisopropyl ether - n-hexane, 53%, mp 144-146 °C. ^{1}H NMR δ: 7.26-7.16 (m, 4H, *ortho*-H and *meta*-H), 5.67 (br s, N-H), 4.38 (dd, J = 3.7 and 9.9 Hz, H-8eq), 3.91 (t, J = 9.1 and 9.9 Hz, H-8ax), 3.15-3.00 (m, 3H, H-5eq, H-5ax and , H-7a) 2.03 (m, H-7eq), 1.93-1.80(m, 2H, H-6eq and H-6ax), 1.52 (m, H-7ax). ^{13}C NMR δ: 144.6 (C-2), 138.6 (*ipso*-C), 128.9 (*meta*-C), 126.0 (*para*-C), 118.8 (*ortho*-C), 68.8 (C-8),55.5 (C-5), 55.1 (C-7a), 25.2 (C-7), 21.3 (C-6). HRMS calcd for $C_{12}H_{14}N_3OCl$, 251.0821; found 251.0825.

2-(4-Chlorophenylimino)-3*N*-methylperhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (13b). The product was chromatographed (silica gel, petroleum ether - EtOAc 60:40, R_f = 0.2) affording an yellowish oil, in 10% yield. ^{1}H NMR δ: 7.12 (m, 2H, *meta*-H), 6.84 (m, 2H, *ortho*-H), 4.03 (dd, J = 4.7 and 10.9 Hz, H-8eq), 3.87 (dd, J = 3.6 and 10.9 Hz, H-8ax), 3.72 (m, H-7a), 3.33 (m, H-5eq), 3.03 (s, 3H, -CH_3) 2.62 (m, H-5ax), 2.01 (m, H-6eq), 1.84 (m, H-7eq), 1.72-1.60 (m, 2H, H-7ax and H-6ax). ^{13}C NMR δ: 153.3 (C-2), 145.8 (*ipso*-C), 128.5 (*meta*-C), 127.2 (*para*-C), 124.5 (*ortho*-C), 68.0 (C-8), 57.7 (C-7a), 52.1, (C5) 28.0 (C-7), 21.9 (C-6).

2-Phenylimino-3*N*-methylperhydropyrrolo[1,2-*d*][1,3,4]oxadiazine (13a). Isothiouronium derivative (**11**)(0.27 g, 0.96 mmol), dissolved in 5 mL of dry THF, was added dropwise to a suspension of NaH (0.2 g, 8 mmol) in 15 mL of dry THF. The reaction was performed under nitrogen. The reaction mixture was heated on an oil bath (60 °C) for 5 h, until no starting material could be observed, as monitored by TLC. A few drops of water was carefully added to the reaction mixture in order to decompose excess sodium hydride, followed by solvent evaporation. Ice-cold water (25 mL) was added to the residue, which was then extracted with chloroform (3 x 40 mL). The organic phase was dried over Na_2SO_4 and the solvent was evaporated off affording an oily product, **13a** (0.22 g; 100%). A small sample was column chromatographed for instrumental analysis (silica gel, petroleum ether - ethyl acetate 65:35, R_f = 0.2). ^{1}H NMR δ: 7.25 (m, 2H, *meta*-H), 6.98-6.94 (m, 3H, *ortho*-H and *para*-H), 4.10 (dd, J = 4.7 and 10.9 Hz, H′-8), 3.91 (dd, J = 3.1 and 10.9 Hz, H′′-8), 3.78 (m, J = 3.1, 4.7, 6.7 and 7.7 Hz, H-7a), 3.38 (m, J = 1.0, 1.7, 6.8 and 8.6 Hz, H′-5), 3.13 (s, 3H, -$C\underline{H}_3$) 2.71 (m, J = 6.3, 8.6 and 11.2 Hz, H′′-5), 2.05 (m, J = 1.0, 2.6, 7.6, 8.0 and 12.8 Hz, H′-6), 1.90 (m, J = 1.7, 2.6, 6.3, 7.9 and 12.6 Hz, H′-7), 1.75 (m, J = 6.7, 7.9, 10.4 and 12.8 Hz, H′′-7), 1.70 (m, J = 6.8, 8.0, 10.4, 11.2 and 12.6 Hz, H′′-6), ^{13}C NMR δ: 153.4 (C-2), 146.7 (*ipso*-C), 128.5 (*meta*-C), 123.3 (*ortho*-C), 122.4 (*para*-C), 68.0 (C-8), 57.8 (C-7a), 52.0 (C-5), 28.2 (C-7), 22.0 (C-6). HRMS calcd for $C_{13}H_{17}N_3O$, 231.1370; found 231.1372.

2-(*N*-Methyl-*N*-phenylamino)perhydropyrido[1,2-*d*][1,3,4]oxadiazine (14a). **7a** was methylated according to earlier described procedures.[3,11] **14a** was purified by column chromatography (silica gel, petroleum ether - ethyl acetae 65:35, R_f = 0.3), affording a light-brown oil (60%). ^{1}H NMR δ: 7.28 (m, 2H, *ortho*-H), 7.10 (m, 2H, *meta*-H), 7.04 (m, 1H, *para*-H), 4.10 (dd, J = 3.4 and 10.2 Hz, H-9eq), 4.03 (t, J = 10 and 10 Hz, H-9ax), 3.39 (m, 1H, H-5eq), 3.17 (s, 3H, -$C\underline{H}_3$), 2.52-2.38 (m, 2H, H-5ax and H-8a), 1.85-1.60 (m, 4H, H-7eq, H-6eq, H-6ax and H-8eq), 1.40-1.17 (m, 2H, H-7ax and H-8ax). ^{13}C NMR δ: 146.9 (C-2), 145.5 (*ipso*-C), 128.7 (*meta*-C), 123.3 (*para*-C), 123.0 (*ortho*-C), 70.4 (C-9), 56.8 (C-5), 55.8 (C-8a), 38.6 (-CH_3), 26.9 (C-8), 25.3 (C-6), 23.4 (C-7). HRMS calcd for $C_{14}H_{19}N_3O$, 245.1526; found 245.1528.

2-(*N*-Chlorophenyl-*N*-Methylamino)perhydropyrido[1,2-*d*][1,3,4]oxadiazine (14b). **7b** was methylated according to earlier described procedures.[3, 11] **14b** was purified by column chromatography (silica gel, petroleum ether - ethyl acetate 65:35, R_f = 0.3), affording a light-brown oil in 67% yield. ^{1}H NMR δ: 7.15 (m, 2H, *meta*-H), 6.95 (m, 2H, *ortho*-H), 4.04 (dd, J = 3.4 and 10.2 Hz, H-9eq), 3.96 (t, J = 10 and 10 Hz, H-9ax), 3.30 (m, 1H, H-5eq), 3.07 (s, 3H, -$C\underline{H}_3$), 2.37 (td, H-5ax), 2.34 (m, H-8a), 1.80-1.55 (m, 4H, H-7eq, H-6eq, H-6ax and H-8eq), 1.30-1.10 (m, 2H, H-7ax and H-8ax). ^{13}C NMR δ: 146.3 (C-2), 144.1 (*ipso*-C), 128.6 (*meta*-C), 128.4 (*para*-C), 123.7 (*ortho*-C), 70.6 (C-9), 56.8 (C-5), 55.7 (C-8a), 38.8 (-CH_3), 26.9 (C-8), 25.4 (C-6), 23.4 (C-7). HRMS calcd for $C_{14}H_{18}ClN_3O$, 279.1134; found 279.1138.

X-RAY CRYSTAL STRUCTURE DETERMINATIONS

Crystal data on **7a**. $C_{13}H_{17}N_3O$, M_r = 231.30, monoclinic, space group $P2_1/C$ (no. 14) a = 8.911(1), b = 13.728

(1) c = 20.895(2) Å, β = 97.15(1)°, V = 2536.0 (5) Å^3 [by least-squares refinement on setting angles (35.6 < 2θ < 41.9°) for 25 carefully centred reflections], Z = 8, D_c = 1.212 g cm^{-3}, F(000) = 992. Colourless prisms, dimensions 0.240 x 0.260 x 0.360 mm, μ(MoK$_\alpha$) = 0.74 cm^{-1}.
Crystal data on **8a**. $C_{14}H_{19}N_3O$, M_r = 245.32, monoclinic, space group $P2_1/C$ (no. 14), a = 6.182(2), b = 9.669(2), c = 22.043(1) Å, β = 91.22 °, V = 1317.2(3) Å^3 [by least-squares refinement on setting angles (39.2 < 2θ < 43.8) for 25 carefully centred reflections], Z = 4, D_c = 1.237 g cm^{-3}, F(000) = 528. Colourless plates, dimensions 0.220 x 0.240 x 0.320 mm, μ(MoK$_\alpha$) = 0.75 cm^{-1}.

Data collection, analysis and refinement. All data were collected at room temperature on a Rigaku AFC5S diffractometer with graphite monochromatized MoK$_\alpha$ (λ = 0.71069 Å) radiation, in the ω-2θ-scan mode, with an ω scan rate of 8° min^{-1} and a scan width of (1.57 + 0.30 tan θ) for **7a** and a scan rate of 4° min^{-1} and a scan width of (1.47 + 0.30 tan θ) for **7a**. The weak reflections [I < 10δ(F)] were rescanned up to two times. The data obtained for **7a** and **8a** were corrected for Lorentz and polarization effects. A total of 4696 unique reflections were measured for **7a** (θ_{max} = 50.0° and R_{int} = 0.039) and a total of 2490 unique reflections for **8a** (θ_{max} = 50° and R_{int} = 0.054). The intensities of three representative check reflections for each compound showed only statistical fluctuations.
Both structures were solved by direct methods[17] and difference Fourier syntheses.[18] Structural parameters were refined by a full-matrix least-squares refinement, non-hydrogen atoms anisotropic, hydrogen atoms with fixed isotropic temperature parameters (1.2 times B_{eq} of the carrying atom). The carbon hydrogens (C-H) were kept in the calculated positions for **7a**, whereas in **8a** all the hydrogens were measured.
In the final cycles, the 2244 data on **7a** with I > 2δ(I) yielded an R value of 0.051 [R_w = 0.034, $w = 1/\delta^2(F_o)$] for 313 parameters; maximum/minimum residual electron density = 0.17/-0.17 e/Å^3. Similarly in the final cycles, the 1618 data on **8a** with I > 3σ(I) yielded an R value of 0.038 (R_w = 0.034, $w = 1/\sigma^2(F_o)$) for 239 parameters; maximum/minimum residual electron density = 0.14/-0.21 e/Å^3.
All calculations were performed with the TEXSAN[19] crystallographic software. Neutral atom scattering and dispersion factors were those included in the program. The Figures were drawn with the ORTEP[20] program.

Table 8. Selected bond distances and angles for 7a

O(1) - C(2)	1.356 (3)	C(2) - O(1) - C(9)	115.6 (3)	O(1) - C(2)- N(3)- N(4)	-4.0 (5)
O(1) - C(9)	1.431 (4)	N(4) - N(3) - C(2)	116.8 (3)	O(1) - C(2)- N(10)- C11()	166.3 (3)
N(3) - N(4)	1.435 (3)	N(3) - N(4) - C(5)	107.1 (2)	O(1) - C(9)- C(8a)- N(4)	55.1 (3)
N(3) - C(2)	1.264 (4)	N(3) - N(4) - C(8a)	111.9 (2)	N(3) - N(4)- C(8a)- C(8)	-179.2 (3)
N(4) - C(5)	1.472 (4)	C(2) - N(10) - C(11)	128.9 (3)	N(3) - N(4)- C(8a)- C(9)	-57.2 (3)
N(4) - C(8a)	1.459 (4)	C(2) - N(10) - H(1)	113 (3)	N(3) - C(2)- O(1)- C(9)	2.2 (5)
N(10) - C(2)	1.377 (4)	O(1) - C(2) - N(3)	128.5 (3)	N(3) - C(2)- N(10)- C(11)	-12.3 (6)
N(10) - C(11)	1.404 (4)	O(1) - C(2) - N(10)	107.8 (3)	N(4) - N(3)- C(2)- N(10)	175.1 (3)
C(8) - C(8a)	1.524 (4)	N(4) - C(8a) - C(8)	110.2 (3)	N(10) - C(2)- O(1)- C(9)	-177.0 (3)
C(8a) - C(9)	1.501 (4)	N(4) - C(8a) - C(9)	107.3 (3)	C(2) - N(10)- C(11)- C(16)	61.3 (3)
		C(8) - C(8a) - C(9)	111.8 (3)	C(5) - N(4)- C(8a)- C(9)	-176.8 (3)
		O(1) - C(9) - C(8a)	111.6 (3)		

Table 9. Selected bond distances and angles for 8a

O(1) - C(2)	1.354 (2)	C(2) - O(1) - C(9)	123.1 (2)	O(1) - C(2)- N(3)- N(4)	-19.3 (3)
O(1) - C(9)	1.453 (2)	N(4) - N(3) - C(2)	120.1 (2)	O(1) - C(2)- N(10)- C11()	1.5 (3)
N(3) - N(4)	1.423 (2)	N(4) - N(3) - C(17)	115.6 (2)	O(1) - C(9)- C(8a)- N(4)	30.0 (3)
N(3) - C(2)	1.365 (2)	C(2) - N(3) - C(17)	120.9 (2)	N(3) - N(4)- C(8a)- C(8)	178.3 (2)
N(4) - C(5)	1.475 (3)	N(3) - N(4) - C(5)	112.1 (2)	N(3) - N(4)- C(8a)- C(9)	-57.0 (2)
N(4) - C(8a)	1.472 (2)	N(3) - N(4) - C(8a)	107.4 (1)	N(3) - C(2)- O(1)- C(9)	-13.0 (3)
N(10) - C(2)	1.277 (2)	C(2) - N(10) - C(11)	121.7 (2)	N(3) - C(2)- N(10)- C(11)	178.9 (2)
N(10) - C(11)	1.411 (2)	O(1) - C(2) - N(3)	116.8 (2)	N(4) - N(3)- C(2)- N(10)	163.1 (2)
C(8) - C(8a)	1.528 (3)	O(1) - C(2) - N(10)	122.5 (2)	N(10) - C(2)- O(1)- C(9)	164.6 (2)
C(8a) - C(9)	1.522 (3)	N(4) - C(8a) - C(8)	109.8 (2)	C(2) - N(10)- C(11)- C(16)	48.6 (3)
		N(4) - C(8a) - C(9)	110.9 (2)	C(5) - N(4)- C(8a)- C(9)	67.3 (2)
		C(8) - C(8a) - C(9)	112.3 (2)		
		O(1) - C(9) - C(8a)	113.6 (2)		

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