123. A(1,3) Strain in *cis*- and *trans*-5,6-Dihydro-4,6-dimethyl-4*H*,8*H*-pyrido[3,2,1-de]phenanthridin-8-ones[1][2])

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Dedicated to the memory of late Prof. Dr. *Hans Schmid*

(16.I.78)

Summary

The stereochemistry of *trans*- and *cis*-2,4-dimethyl-tetrahydroquinolines, **6** and **7** were derived from ^{1}H-NMR. studies. These were converted respectively into *trans*- and *cis*-5,6-dihydro-4,6-dimethyl-4*H*,8*H*-pyrido[3,2,1-de]phenanthridin-8-ones **18** and **20** by a *Pschorr* reaction on the anthranilamides **10** and **15**. Bromophenanthridones **19** and **21** were similarly prepared from bromoanthranilamides **12** and **17**. Detailed ^{1}H-NMR. studies on **18** and **20** indicated axial disposition of the methyl groups at C(2) in both compounds in contrast to the situation in **6** and **7**. This is presumably to avoid adverse CH_3CO group interaction of the A(1,3) type. The severity of this is gauged by the preference of **20** for a normally forbidding 1,3-diaxial orientation of two methyl groups. X-ray crystallographic studies on **19** and **20** confirm the stereochemical assignments.

In an earlier paper [1] of this series, we had shown that restricted rotation of the amide bond in cyclic amides having partial structures **1** leads to allylic strain of the A(1-3) type [2] [3], resulting in the group R occupying preferentially the axial position when present on a piperidine ring. NMR. and X-ray crystallographic evidence were adduced to demonstrate this in the case of *N*-benzoyltetrahydroquinaldine **2** [4], pyridobenzoxazepinone **3** [5], pyridobenzoxazinone **4** [6] and pyridophenanthridone **5** [7]. In these molecules the methyl group had the axial conformation whereas it was equatorially placed in the tetrahydroquinaldine precursors. The study revealed additionally that in **2** and **3** with some measure of

[1]) Contribution No. 500 from *Ciba-Geigy* Research Centre.

[2]) Presented in part before the National Conference on Crystallography, December 4-6, 1975, National Physical Laboratory, New Delhi 110012.

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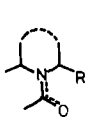
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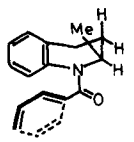
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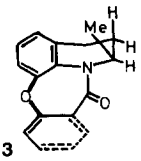
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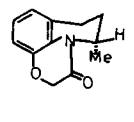
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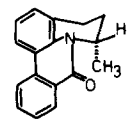
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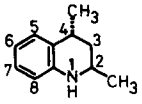
flexibility, the tetrahydropyridine existed as a slightly distorted boat, while in **4** and **5**, the polycyclic framework was rigid and the tetrahydropyridine ring was in a half-chair conformation. The equatorial methyl-carbonyl inter-action was larger than 0.5 kcal/mol, the value for axial methyl hydrogen interaction [1]. It was proposed to study a derivative of **1** with an extra methyl group at position 4 of the tetrahydroquinoline moiety, *cis* to the one at C(2) [1]. The present paper reports on the synthesis of *cis*- and *trans*-5,6-dihydro-4,6-dimethyl-4*H*,8*H*-pyrido[3,2,1-de]-phenanthridones **20** and **18** respectively and their conformational studies by NMR. spectroscopy and X-ray crystallography.

The requisite starting materials, 2,4-dimethyl-1,2,3,4-tetrahydroquinolines **6** and **7** have been prepared earlier from 2,4-dimethylquinoline by reduction with sodium/alcohol [8], but their stereochemistry was not assigned. This has been done now by a study of their 100-MHz-NMR. spectra with extensive decoupling. Chemical shift and coupling data of the chlorhydrates of **6** and **7** with m.p. 162–163° and 226–227° respectively, in $CDCl_3$ solution are presented in *Table 1*[6]). The proton at C(2) in **6** was a *m* at 3.76 ppm, reduced to a $d \times d$ upon decoupling from the neighbouring methyl group at 1.70 ppm. *J* values of 9 and 2 Hz for the coupling of C(2) proton with the adjacent protons at C(3) indicate axial disposition of the former, placing the methyl group in the equatorial position. The signal of the proton at C(4) was again a *m* at 3.10 ppm which became a $d \times d$ ($J = 4$ and 6 Hz) upon decoupling of the related methyl group at 1.35 ppm, indicating equatorial and axial positions of the proton and methyl group respectively at this centre. **6** was thus seen to be *trans*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline with conformation **6a**. This is presumably preferred to the alternative **6b**, because the latter has a *peri* H–C(3)/H_3C–C(4) interaction while both **6a** and **6b** have one diaxial CH_3/H interaction.

The NMR. spectrum of **7** · HCl, m.p. 226–227°, was similarly run in $CDCl_3$. The *m* due to H–C(2) at 3.58 ppm was decoupled from the methyl group at 1.74 ppm to give a $d \times d$. The vicinal coupling constants were 9 and 3 Hz, indicating an axial position of H–C(2). The *m* due to H–C(4) at 3.06 ppm likewise became a $d \times d$ upon irradiation of its neighbouring CH_3 group at 1.38 ppm; the vicinal coupling constants of 11 and 6 Hz suggest an axial position of H–C(4). **7** was thus believed to be *cis*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline with the two methyl groups in a *cis*-diequatorial orientation **7a**. The alternative **7b** lacks the *peri* H–C(3)/H_3C–C(4) interaction of **7a**, but has a forbidding 1,3-diaxial disposition of two methyl groups.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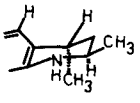
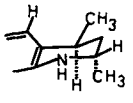

6a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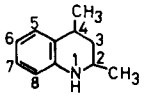
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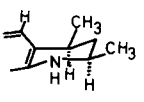
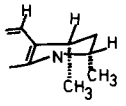
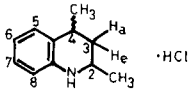
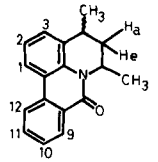

7a


7b

[6]) All spectra were analysed first order.

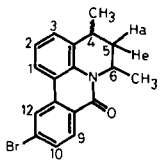
Table 1. *Chemical shift, coupling constant data for* 

Compound	Chemical shifts (ppm) (multiplicity) of protons at						CH_3 at		Coupling constants (Hz) of						
	C(8)	C(5), C(6), C(7)	C(2)	C(4)	$C(3)_a$	$C(3)_e$	C(2)	C(4)	H–C(2) with CH_3	H_a–C(3)	H_e–C(3)	CH_3	H–C(4) with H_a–C(3)	H_e–C(3)	gem. at C(3)
6 (*trans*)	7.66 (*m*)	7.1–7.5 (*m*)	3.76 (*m*)	3.10 (*m*)	2.32 (*m*)	1.88 (*m*)	1.70 (*d*)	1.35 (*d*)	7	9	2	7	6	4	– 14
7 (*cis*)	7.66 (*m*)	7.1–7.5 (*m*)	3.58 (*m*)	3.06 (*m*)	1.90 (*m*)	2.14 (*m*)	1.74 (*d*)	1.38 (*d*)	7	9	3	7	11	6	– 14

Table 2. *Chemical shift, coupling constant data for* 

Compound	Chemical shift (ppm) (multiplicity) of protons at								CH_3 at		Coupling constants (Hz) of						
	C(9)	C(1), C(12)	C(3), C(10), C(11)	C(2)	C(6)	C(4)	$C(5)_a$	$C(5)_e$	C(6)	C(4)	H–C(6) with CH_3	H_a–C(3)	H_e–C(3)	CH_3	H–C(4) with H_a–C(3)	H_e–C(3)	gem. at C(3)
18 (*trans*)	8.56 ($d\times d$)	8.06–8.36 (*m*)	7.4–7.8 (*m*)	7.22 (*t*)	5.44 (*m*)	3.24 (*m*)	1.76 (*m*)	2.06 (*m*)	1.36 (*d*)	1.44 (*d*)	7	5.5	2.5	7	12	5.5	– 14
20[a]) (*cis*)	8.56 ($d\times d$)	8.05–8.30 (*m*)	7.32–7.80 (*m*)	7.20 (*t*)	5.42 (*m*)	3.12 (*m*)	2.32[b]) (*m*)	1.94[b]) (*m*)	1.58 (*d*)	1.46 (*d*)	7	6.0	2.5	7	6.4	2.5	– 14

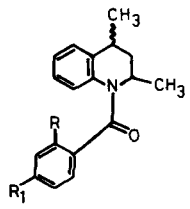
[a]) $J_{H-C(4),H-C(6)} = 2$ Hz. [b]) Assignments tentative; reversal not ruled out.

Table 3. *Chemical shift data for* 

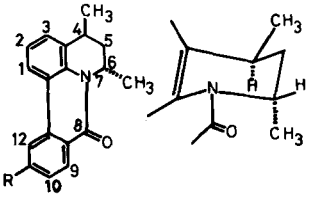
Compound	Chemical shift (ppm) (multiplicity) of protons at									CH_3 at	
	C(9)	C(12)	C(1)	C(3), C(10)	C(2)	C(6)	C(4)	$C(5)_a$	$C(5)_e$	C(6)	C(4)
19 (*trans*)	8.37 (*d*)	8.28 (*d*)	7.97 ($d\times d$)	7.3–7.75 (*m*)	7.17 (*t*)	5.35 (*m*)	3.20 (*m*)	1.78 (*m*)	2.07 (*m*)	1.30 (*d*)	1.42 (*d*)
21 (*cis*)	8.32 (*d*)	8.23 (*d*)	7.87 ($d\times d$)	7.1–7.75 (*m*)	7.10 (*t*)	5.33 (*m*)	3.07 (*m*)	2.34 (*m*)	1.87 (*m*)	1.52 (*d*)	1.39 (*d*)

Having deduced the stereochemistry of the dimethyl-tetrahydroquinoline substrates, we proceeded to build up the pyridophenanthridones **18–21** through the route described earlier [7]. **6** was thus converted to the 2-nitrobenzoyl derivative **8** which was reduced to the amine **10**. A *Pschorr*-type cyclization of the diazonium compound from **10** gave besides the phenol **11**, the desired *trans*-pyridophenanthridone **18**. The nitrobromobenzamide **9** of **6** was processed similarly to afford the *trans*-dimethyl- bromophenanthridone **19** through the amine **12**. Similar manipulations on the 2-nitrobenzamide **13** and the bromonitrobenzamide **14** in the *cis*-series led through amines **15** and **17** to the formation of the *cis*-dimethyl-pyridophenanthridone **20** and its bromo derivative **21**. The phenol **16** was a by-product in the formation of **20**. Chemical shifts and coupling data from the 100-MHz-NMR. spectra in $CDCl_3$ of **18** and **20** and 60-MHz-spectra of **19** and **21** are reported in *Tables 2* and *3* respectively.

In the 100-MHz-NMR. spectrum of **18**, H–C(6) shows a *m* at 5.44 ppm. This was simplified to a $d \times d$ upon irradiation of the neighbouring methyl group at 1.36 ppm. Vicinal coupling values of 5.5 Hz with H_a–C(5) and 2.5 Hz with H_e–C(5) were obtained from the decoupled spectrum. H–C(6) must therefore be equatorial and the methyl group axial. The *m* due to H–C(4) at 3.24 ppm was again transformed into a $d \times d$, with vicinal *J* values of 12 Hz with H_a–C(5) and 5.5 Hz with H_e–C(5) respectively, after decoupling from the H_3C–C(4) at 1.44 ppm.

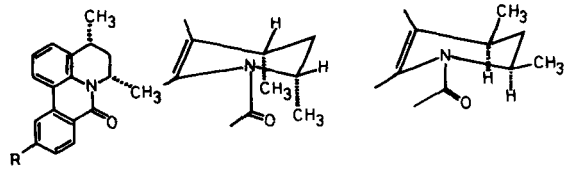


trans-series	R	R_1	*cis*-series
8	NO_2	H	**13**
9	NO_2	Br	**14**
10	NH_2	H	**15**
11	OH	H	**16**
12	NH_2	Br	**17**



18 R = H
19 R = Br

18a,19a **18b**



20 R = H
21 R = Br

20a,21a **20b**

The conclusion can thus be reached that H–C(4) and H_3C–C(4) are respectively axially and equatorially oriented. The stereochemistry of **18** is consequently **18a**, with the tetrahydropyridine in a half-chair, with the methyl groups occupying reverse positions compared to the situation in the starting material **6a**. This is clearly a consequence of potential adverse A(1,3) type interaction of an equatorially oriented methyl group at C(2) and the oxygen atom of coplanar CO group. This is estimated to be 7.7 kcal/mol and the *peri* interaction of H–C(3)/H_3C_e–C(4) present in **18a**, but absent in **6a**, 1 kcal/mol. Considering that there is one 1,3-diaxial H/CH_3 interaction in either conformation of the tetrahydropyridine half-chair in **18**, **18a** would be favoured over **18b** by 6.7 kcal/mol[7]). **19** would then have the conformation **19a**, which was confirmed by the strong similarity of its NMR. spectrum to that of **18** between 0 and 5.5 ppm. In the NMR. spectrum of the *cis*-pyridophenanthridone **20**, the signal due to H–C(6) was a *m* at 5.42 ppm and after decoupling from the neighbouring methyl group at 1.58 ppm, showed vicinal coupling with H–C(5) and a long range coupling of the order of 2 Hz with H–C(4). The desired *J* values could however be obtained by irradiation of the signal due to H–C(4) at 3.12 ppm and scrutiny of the signals due to protons at C(5). For the latter, geminal coupling of -14 Hz and vicinal couplings, H_{eq}–C(5)/H–C(6), 2.5 Hz and H_a–C(5)/H–C(6) of 6.0 Hz were then obtained, showing thereby that the proton at C(6) was equatorial and *hence the methyl group axial.* The signals of H–C(4) were a *m* at 3.12 ppm and decoupling from the neighbouring methyl group at 1.46 ppm revealed vicinal couplings and a long-range coupling (with H–C(4)). Irradiation of H–C(6) and examination of the splitting pattern of protons at C(5) allowed the extraction of vicinal *J* values of 2.5 Hz for H_e–C(5)/H–C(4) and 6.4 Hz for H_a–C(5)/H–C(4). This allowed the placement of H–C(4) in the equatorial and methyl group in the axial position. The stereochemistry of **20** can thus be deduced to be **20a**, with the tetrahydropyridine in a half-chair conformation but with *the methyl groups diaxially located* in contrast to the starting material **7**. The long-range coupling between protons at C(4) and C(6) would imply they are in W conformation, thus additionally corroborating conformation **20a**. **7a** has a *peri* H–C(3)/H_3C–C(4) interaction, which is replaced in **20a** by a 1,3-diaxial CH_3/CH_3 interaction. On the basis of a value of 3.2 kcal/mol[7]) for the diaxial CH_3/CH_3 interaction, it can be computed that conformation **20a** will be favoured over **20b** by $7.7+1.0-3.2=5.5$ kcal/mol. Common derivation from **7** and NMR. spectral similarity allows one to assign conformation **21a** to the bromopyridophenanthridone **21**. These spectroscopic deductions were confirmed by X-ray crystallographic studies reported below. In the *trans*-series, **19** gave suitable crystals but in the *cis*-series, the light atom compound **20** crystallized well.

X-Ray crystallographic studies. – The crystals of **19** and **20** were obtained by slow evaporation of alcoholic solutions. The data for the *trans* compound **19** were collected on an automatic diffractometer (R.P.). A total of 2083 reflections were scanned by $\zeta/2W$ technique with CuK_a radiation. Out of these, 1497 were judged to be above the background and were used in the determination of the structure. For the *cis* compound, data were collected by multiple film, equi-inclination *Weisenberg* photographs *(M.R.N. & K.V.).* A total of 713 reflections were visually estimated with a calibrated strip. The unit cell

[7]) These values were derived from potential energy calculations incorporated in the Ph.D. thesis of *M.R.N.*

constants were obtained from the *Weisenberg* and precession photographs taken with CuK_α radiation. Crystal data for the compounds **19** and **20** are recorded in *Table 4.*

The structure of the *trans* compound **19** was solved by the heavy atom technique and has been refined by full-matrix least-squares method to a final R-value of 7.4% for 1497 reflections. The structure of the *cis* compound was solved using the programme MULTAN [9] modified [10] to suit an *IBM* 360/44 computer with 64 kilobytes core memory. It may be mentioned that the linearity of the *Wilson* curve increased significantly when spherically averaged molecular scattering factors were used. 250 reflections with $|E| \geq 1.36$ were used for structure solution. The positional and anisotropic thermal parameters were refined by the least-squares method using the block diagonal approximation to an R-value of 11.4% for 713 observed reflections[8]).

The bond lengths and angles of the *trans* molecule **19** are shown in *Figures 1a* and *1b* respectively. The bond lengths and angles of the *cis* molecule **20** are shown in *Figures 2a* and *2b.* Some torsion angles of interest are recorded in *Table 5.* Perspective views of the *trans* and *cis* compounds are shown in *Figures 3* and *4* respectively. *The numbering of atoms is arbitrary.*

Table 4. *Crystal data for* **19** *and* **20**

	19	**20**
Chemical formula	$C_{18}H_{16}BrNO$	$C_{18}H_{17}NO$
Crystal system	Monoclinic	Monoclinic
Cell constants	$a = 20.693$ Å	$a = 8.57$ Å
	$b = 10.737$	$b = 11.54$
	$c = 6.766$	$c = 14.54$
	$\beta = 94.68°$	$\beta = 108.0°$
Space Group	$P2_1/_n$	$P2_1/_c$
(Determined uniquely by space group extinctions)		
D_m (method of flotation)	1.50 g/cm^3	1.28 g/cm^3
D_c (for $Z = 4$)	1.51 g/cm^3	1.29 g/cm^3

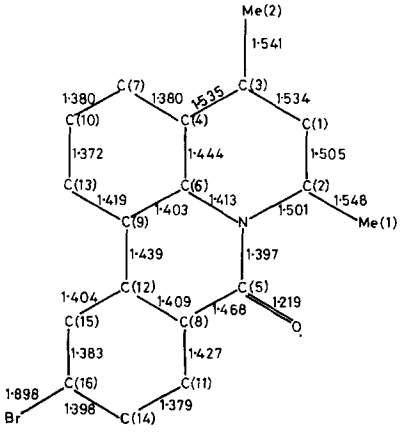


Fig. 1a. *Bond lengths* (Å) *of the* trans *derivative* **19**

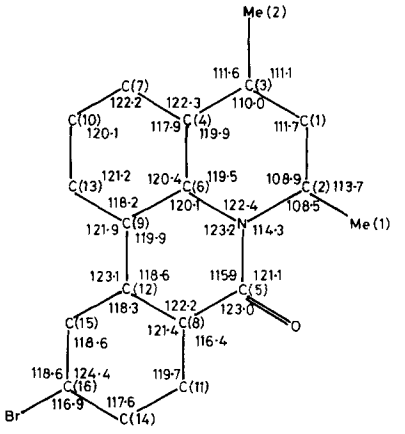


Fig. 1b. *Bond angles* (°) *of the* trans *derivative* **19**

[8]) Data on the final positional parameters of **19** and **20** are available from *K.V.* on request.

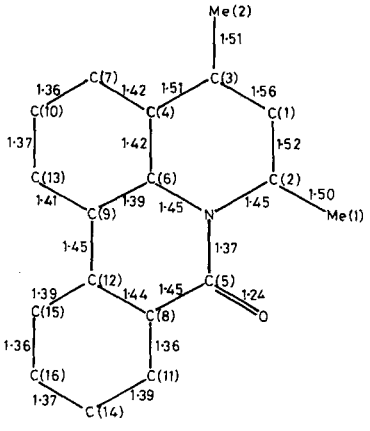


Fig. 2a. *Bond lengths* (Å) cis *derivative* **20**

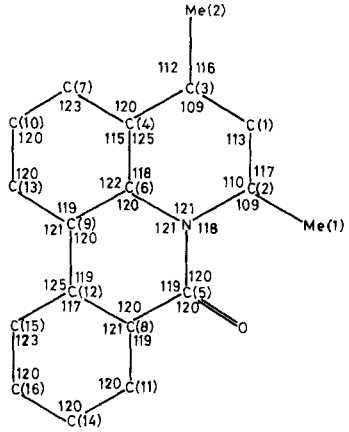


Fig. 2b. *Bond angles* (°) *of the* cis *derivative* **20**

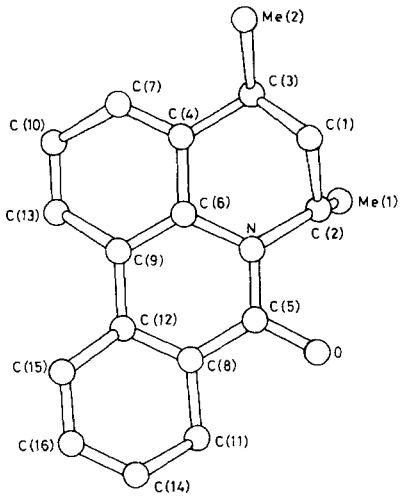


Fig. 3. *Perspective view of the* trans-*isomer* **19** (the bromine bonded to C(16) is not shown)

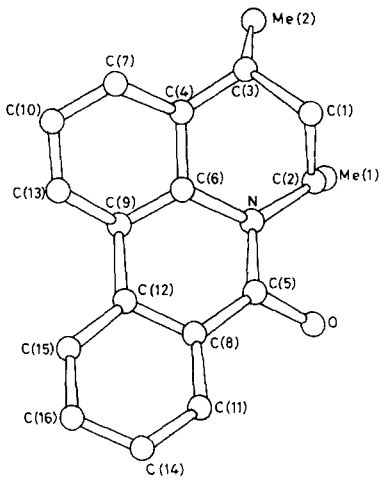


Fig. 4. *Perspective view of the* cis-*isomer* **20**

Comparison of the torsion angles within the tetrahydropyridine rings of both the compounds with the corresponding values of C_2 symmetric half-chair conformation of cyclohexene *(Table 6)* shows that the tetrahydropyridine ring in both the compounds possesses a half-chair conformation. The smaller value for the torsion angle C(4)–C(6)–N–C(2) in both the compounds indicates that the rings in these molecules are slightly flattened compared to cyclohexene. The conformation of the *trans* compound is very nearly the 1,6 diplanar conformation [11] of cyclohexene. From the torsion angles C(6)–N–C(2)–Me(1) and

Table 5. *Some important torsion angles* (in degrees)

Torsion angle	*cis*-Compound (**20**)	*trans*-Compound (**19**)
C(2)–N–C(5)–C(8)	173	178
C(2)–N–C(5)–O	– 3	– 2
C(6)–N–C(5)–C(8)	– 4	1
C(6)–N–C(5)–O	– 180	– 178
C(6)–C(9)–C(12)–C(8)	– 1	4
C(6)–C(9)–C(12)–C(15)	– 179	– 176
C(13)–C(9)–C(12)–C(8)	176	– 177
C(13)–C(9)–C(12)–C(15)	– 2	4
C(11)–C(8)–C(5)–O	– 3	– 1
C(12)–C(8)–C(5)–O	174	179
C(6)–N–C(2)–Me(1)	91	93
C(5)–N–C(2)–Me(1)	– 86	– 84
C(3)–C(1)–C(2)–Me(1)	– 67	– 63
C(2)–C(1)–C(3)–Me(2)	81	– 179
C(6)–C(4)–C(3)–Me(2)	– 114	149
C(7)–C(4)–C(3)–Me(2)	71	– 32

Table 6. *Comparison of the torsion angles (degrees) within the tetrahydropyridine with the symmetric conformation of cyclohexene*

Compound	1-2	2-3	3-4	4-5	5-6	6-1
Cyclohexene	0	15	– 45	62	– 45	15
19	4	25	– 55	57	– 32	2
20	1	15	– 45	58	– 39	9

C(2)–C(1)–C(3)–Me(2) *(Table 6)* it is evident that the methyl groups Me(1) and Me(2) are axially oriented in the *cis* compound, whereas Me(1) is axial and Me(2) equatorial in the *trans* compound. The equatorial substituent at C(2) suffers an A(1,3) type of interaction [2] with the oxygen atom and an equatorial substituent at C(3) experiences an A(1,2) interaction [2] with C(7). The observed conformation of the *trans* compound indicates that the A(1,3) interaction is energetically more unfavourable than the A(1,2) type interaction. The intramolecular distance between the carbonyl oxygen atom and Me(1) is 3.201 Å and between Me(2) and C(7) is 2.940 Å. The observed conformation of the *cis* compound shows that the sum of A(1,3) and A(1,2) interactions is stronger than the 1,3 diaxial Me ... Me interaction. The methyl group of C(2) is at a distance of 3.25 Å from the carbonyl oxygen, the distance between Me(2) and C(7) is 3.17 Å and that between the diaxial methyl groups, 3.30 Å. The widening of angles C(1)–C(2)–Me(1) (= 117°) and C(1)–C(3)–Me(2) (= 116°) in the *cis* compound must be attributed to the repulsion between the diaxial methyl groups.

NMR. evidence has been used to show that in *cis*-1,3,5-trimethyl-4-nitrosopiperazine, the methyl groups at C(3) and C(5) occupy axial positions [12]. This is a consequence of the restricted rotation of the N–N bond resulting in A(1,3) strain due to O ... CH_3 interaction. Again in 1,4-dinitroso-2,3,5,6-tetramethylpiperazine, all the methyl groups have been assigned axial positions using NMR. data,

although *Johnson* [2] speculates that the molecule may exist largely in a twist boat rather than chair conformation. We believe that we have dramatic evidence for the severity of A(1,3) strain in molecules **19** and **20**, demonstrated unequivocally by X-ray studies.

Experimental Part

Melting points (m.p.) are uncorrected. UV. spectra (nm (log ε)) were run on a *Beckman* DK2A spectrophotometer, using 95% solutions in ethanol. IR. spectra were run on *Perkin Elmer* Infra cord. NMR. spectra refer to proton spectra from a *Varian* A60 or HA 100 spectrometer. Chemical shifts are quoted in ppm downfield from TMS used as internal reference. Mass spectra are from a *Varian* Mat CH 7 mass spectrometer.

cis- *and* trans-*2,4-Dimethyl-1,2,3,4-tetrahydroquinolines.* To 10 g 2,4-dimethylquinoline in 250 ml abs. ethanol was added, during 1 h, 15 g sodium metal in small pieces. The solution was heated for a further 1 h on an oil bath (bath temp. 150°), and stripped of alcohol *in vacuo.* Water and ether were added to the residue. The ether layer was separated, washed with water, dried and evaporated to give 10.2 g oil. This was shaken with 10 g benzoyl chloride and 50 ml 10% aqueous NaOH-solution for 15 min. The product was extracted into ether and the ether layer washed first with 2N HCl and then water. Drying and evaporation gave 10 g which became crystalline with ether/hexane. Recrystallization gave the benzoyl derivative of *cis*-dimethyltetrahydroquinoline; 3.3 g, m.p. 112–114°. The mother liquors on evaporation gave 6.6 g oil which was heated with 50 ml 6N HCl under reflux for 2 days. The cooled solution was freed from neutral material by extraction with ether and then evaporated to a small volume. Basification with strong aqueous NaOH-solution and ether extraction gave 4.1 g oily mixture of *cis-* and *trans*-2,4-dimethyltetrahydroquinolines which was acetylated with 6 ml acetic anhydride and 6 ml pyridine at 100° for 3 h. The crude acetyl derivative was crystallized from alcohol to give trans-N-*acetyl-2,4-dimethyl-1,2,3,4-tetrahydroquinoline:* 0.9 g, m.p. 93–95°.

Hydrolysis of 3.3 g cis-N-*benzoyl-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* by reflux with 30 ml 6N HCl for 2 days and evaporation gave *cis*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**7**)·HCl (from EtOH): 2 g, m.p. 226–227°.

$C_{11}H_{16}ClN$ (197.7) Calc. C 66.80 H 8.16 N 7.08% Found C 66.75 H 8.50 N 7.25%

Free base, b.p. 120°/1–1.5 Torr.

Hydrolysis of 0.9 g trans-N-*acetyl-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* with 15 ml 6N HCl and 10 ml dioxane under reflux for 3½ h gave upon work-up *trans*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**6**): 0.7 g, b.p. 120–130°/2 Torr; chlorhydrate (from EtOH/Et_2O), m.p. 162–163°.

$C_{11}H_{16}ClN$ (197.7) Calc. C 66.80 H 8.16 N 7.08% Found C 66.87 H 8.40 N 7.14%

cis-*4,6-Dimethylpyridophenanthridone series.* – cis-N-*(2-Nitrobenzoyl)-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* (**13**). To a stirred mixture of 5.4 g *cis*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**7**) in 50 ml ether and 8.5 g $NaHCO_3$ in 50 ml water was added 2-nitrobenzoyl chloride (obtained by refluxing 5.7 g 2-nitrobenzoic acid and 60 ml $SOCl_2$ for 4 h) in 30 ml ether. After 3 h, the mixture was filtered off to give 8.1 g product. The ether layer in the filtrate was worked up to give 0.4 g additional neutral product; total yield of **13** (from EtOH): 8.5 g, m.p. 183–185°.

$C_{18}H_{18}N_2O_3$ (310.3) Calc. C 69.66 H 5.85 N 9.05% Found C 69.70 H 6.13 N 9.02%

The corresponding *2-nitro-4-bromobenzamide* (**14**) was similarly prepared from 0.9 g amine and 1.35 g acid; yield: 1.7 g (from EtOH), m.p. 170–171°.

$C_{18}H_{17}BrN_2O_3$ (389.3) Calc. C 55.54 H 4.40 N 7.20% Found C 55.53 H 4.55 N 7.28%

cis-N-*(2-Aminobenzoyl)-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* (**15**). 8.5 g **13** was hydrogenated in 450 ml MeOH at atmospheric pressure and room temperature using 0.2 g PtO_2 till absorption of

hydrogen was complete. Evaporation gave 6.9 g crystalline product, which was recrystallized from hexane to give **15**, m.p. 107–109°.

$C_{18}H_{20}N_2O$ (280.4) Calc. C 77.11 H 7.19 N 9.99% Found C 77.11 H 7.40 N 10.18%

Similar catalytic reduction of the corresponding N-*(2-nitro-4-bromobenzoyl)* derivative **14** gave the desired amine **17** in very low yield. A better yield was realized by using iron and alcohol for reduction. Thus 1 g nitrobenzamide **14** and 3 g iron powder suspended in 20 ml alcohol containing 2 drops of conc. hydrochloric acid were heated together under reflux for 2 h. The mixture was filtered and the filtrate evaporated to give the aminobenzamide **17** (from Et_2O/hexane): 0.6 g, m.p. 133–135°.

$C_{18}H_{19}BrN_2O$ (359.3) Calc. C 60.17 H 5.33 N 7.80% Found C 60.66 H 5.51 N 7.71%

cis-*4,6-Dimethylpyridophenanthridones* **20** *and* **21**. 2.8 g **15** was dissolved in 40 ml AcOH and 3.5 ml conc. sulfuric acid. The solution was cooled to $-5°$ and treated under stirring with 0.8 g sodium nitrite in 10 ml water. After 1 h at $-5°$, 0.3 g urea and 65 ml 2N H_2SO_4 were added and the mixture heated at 100° for 30 min. This was followed by the addition of 5 g zinc dust and further heating for 30 min. The mixture was filtered and the filtrate diluted with water and extracted with 100 ml chloroform. The chloroform layer was evaporated and the residual oil (2.5 g) taken into ether and separated through aqueous NaOH-solution into phenolic and neutral products. The phenolic part weighed 0.5 g and was crystallized from hexane and then from EtOH to give cis-N-*(2-hydroxybenzoyl)-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* (**16**): 0.35 g, m.p. 168–169°.

$C_{18}H_{19}NO_2$ (281.3) Calc. C 76.84 H 6.81 N 4.98% Found C 77.12 H 6.88 N 5.25%

The neutral product became crystalline with hexane to give the *cis*-dimethylpyridophenanthridone **20**, 1.9 g, m.p. 94–97° which was recrystallized again from hexane to give 1.2 g, m.p. 99–100°. – IR. (Nujol): 1650 (C=O). – UV.: 230 (inflex) (4.59), 235 (4.61), 240 (inflex) (4.55), 255 (inflex) (4.21), 264 (4.31), 305 (inflex) (3.71), 315 (inflex) (3.72), 326 (3.86), 340 (3.81).

$C_{18}H_{17}NO$ (263.3) Calc. C 82.10 H 6.51 N 5.32 Found C 82.40 H 6.78 N 5.35%

Diazotisation-cyclization of 1 g **15** gave the bromophenanthridone (**21**): 0.7 g, m.p. 144–147° raised to 150–152° by crystallization from EtOH. – UV.: 236 (inflex) (4.65), 243 (4.68), 267 (4.32), 305 (inflex) (3.69), 317 (inflex) (3.74), 328 (3.82), 343 (3.77). – MS.: 343 [M^+, Br^{81}], 341 [M^+, Br^{79}].

$C_{18}H_{16}BrNO$ (342.2) Calc. C 63.17 H 4.71 N 4.09% Found C 62.92 H 5.06 N 4.09%

trans-*4,6-Dimethylpyridophenanthridone series.* – trans-N-*(2-Nitrobenzoyl)-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* (**8**). 4.2 g *trans*-2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**6**) and the acid chloride from 4.35 g 2-nitrobenzoic acid gave the nitrobenzamide **8**: 5.7 g (from MeOH), m.p. 160–162°.

$C_{18}H_{18}N_2O_3$ (310.3) Calc. C 69.66 H 5.85 N 9.03% Found C 69.65 H 6.23 N 9.34%

1.6 g of the same tetrahydroquinoline and 2.46 g 2-nitro-5-bromobenzoic acid gave the *amide* **9**: 2.9 g (from EtOH), m.p. 152–154°.

$C_{18}H_{17}BrN_2O_3$ (389.3) Calc. C 55.54 H 4.40 N 7.02% Found C 55.69 H 4.76 N 7.18%

trans-N-*(2-Aminobenzoyl)-2,4-dimethyl-1,2,3,4-tetrahydroquinoline* (**10**). Reduction of 5.7 g amide **8** in 350 ml MeOH using 0.2 g PtO_2 and hydrogen at atmospheric pressure and room temp. gave the aminobenzoyl derivative **10**: 4.5 g (from hexane), m.p. 95–97°.

$C_{18}H_{20}N_2O$ (280.4) Calc. C 77.11 H 7.19 N 9.99% Found C 77.12 H 7.30 N 10.15%

Similar reduction of 2.7 g nitrobromobenzamide **9** gave the *aminobromobenzamide* **12**, characterized as chlorohydrate: 0.8 g (from EtOH/Et_2O), m.p. 181–184°.

$C_{18}H_{19}BrN_2O \cdot HCl$ (395.7) Calc. C 54.63 H 5.09 N 7.08% Found C 54.80 H 5.55 N 7.27%

trans-*4,6-Dimethylpyridophenanthridones* **18** *and* **19**. Treatment of 2.8 g amine **10** with nitrous acid as before gave the phenolic amide **11**: 0.5 g (from hexane), m.p. 103–104°

$C_{18}H_{19}NO_2$ (281.3) Calc. C 76.84 H 6.81 N 4.98% Found C 77.22 H 6.99 N 5.31%

and the *trans*-4,6-dimethylpyridophenanthridone **18**: 1.3 g (from EtOH), m.p. 135–137°. – IR. (Nujol): 1655 (C=O). – UV.: 230 (inflex) (4.59), 235 (4.63), 240 (inflex) (4.58), 253 (inflex) (4.20), 263 (4.31), 303 (inflex), (3.71), 315 (inflex) (3.74), 326 (3.88), 340 (3.83).

$C_{18}H_{17}NO$ (263.3) Calc. C 82.10 H 6.51 N 5.32 Found C 82.40 H 6.84 N 5.60%

Diazotisation-cyclization of 0.8 g **12** gave the pyridophenanthridone **19**: 0.15 g (from EtOH), m.p. 145–147°. – UV.: 236 (inflex) (4.65), 244 (4.69), 268 (4.31), 305 (inflex) (3.69), 317 (inflex) (3.73), 329 (3.83), 343 (3.78). – MS.: 343 (M^+, Br^{81}), 341 (M^+, Br^{79}).

$C_{18}H_{16}BrNO$ (342.2) Calc. C 63.17 H 4.71 N 4.09% Found C 63.53 H 4.96 N 4.24%

K.N. and *R.K.S.* thank Prof. *T.R. Govindachari* and Dr. *R.S. Grewal*, past and present Directors respectively of *Ciba-Geigy* Research Centre for their encouragement and Dr. *S. Selvavinayakam* and his associates for analytical and spectral data. *K.V.* and *M.R.N.* wish to thank the *CSIR* (India) for financial assistance.

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