79. The Structure of Pyroergotamine

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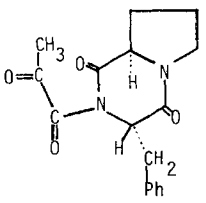
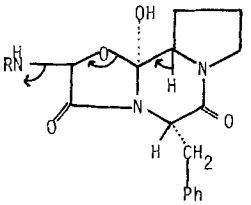
(17.XI.84)

The molecular structure of pyroergotamine has been determined by single-crystal X-ray diffraction analysis to be the pyruvoyldiketopiperazine **1**. The diketopiperazine ring exists in a folded or boat conformation, with a dihedral angle of 40° between the two almost planar peptide units. The R-group of the phenylalanine residue occupies a quasi-axial position of the diketopiperazine ring, while that of the proline residue is in a quasi-equatorial position. Puzzling spectroscopic and chemical properties of the compound can be rationalised in terms of crowding within the molecule.

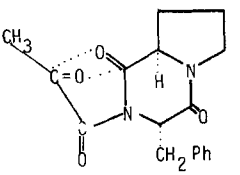
Although the structures of the peptide portions of ergotamine and the related ergot alkaloids were determined over 30 years ago [1], structures for the peptide products obtained by thermal cleavage [2] of the dihydroalkaloids **2** have remained a puzzle[2]). The



1



2 R = Dihydrolysergoyl



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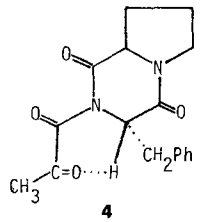

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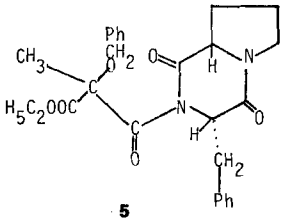

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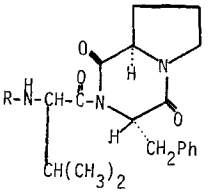


6a R = lysergoyl
6b R = dihydrolysergoyl

[1]) Deceased.

[2]) *Rucman* and *Stanovnik* [3] recently described the thermal decomposition of dihydroergocristine methanesulfonate between 80° and 190 °C. The products, obtained after dissolution in aq. NaOH followed by extraction with CH_2Cl_2 were dihydrolysergoyldehydrovaline methyl ester, the corresponding azolactone, dihydrolysergic acid and its amide, and the (*S,S*)- and (*S,R*)-phenylalanylproline lactams. No compound corresponding to **1** was detected, presumably because, if present, it would have decomposed during the treatment with base.

compounds were readily hydrolysed to the corresponding diketopiperazine (DKP) and pyruvic or dimethylpyruvic acid, but did not undergo catalytic reduction [1] as expected for a pyruvoyldiketopiperazine **1**. *Stoll* and *Hofmann* [4] abandoned a dioxacyclobutane structure [1] in favour of structure **3**[3]) in which the dotted lines indicate intramolecular interactions which modity the properties of the ketone group. The syntheses of the cleavage products [5] [6] supported the pyruvoyldiketopiperazine structure (**1** or **3**), but were inconclusive because they both involved the use of high temperatures in the final stages. *Green* and *Lucken* [7] reported that the NMR spectrum of pyroergotamine was consistent with a pyruvoyldiketopiperazine structure except that the signal for the α-proton of phenylalanine appeared as a triplet at 5.08 ppm; they accounted for the downfield shift of about 0.8–0.9 ppm relative to the corresponding DKP in terms of a remarkable H-bonding effect (see **4**). Such an explanation does not account for the similar low-field shift ($\delta = 5$ ppm) shown by the corresponding proton in compounds **5** [8] and **6a** and **b** [9]. Clearly the effect in **1** is due to the imide, and not the ketone carbonyl in the side chain. We now report the structure determination of pyroergotamine by X-ray crystallography and ^{1}H- and ^{13}C-NMR spectroscopy.

Results and Discussion. – *X-Ray Studies.* The X-ray crystallographic results show that pyroergotamine has structure **1** *(Fig. 1)*. The final coordinates and anisotropic thermal parameters for all atoms are listed in *Table 1*. The labelling scheme used in all tables to designate the atoms of the pyroergotamine molecule is given in *Fig. 1*. Bond lengths and angles for the entire molecule are listed in *Table 2;* values for the non-H-atoms are shown pictorially in *Fig. 2*.

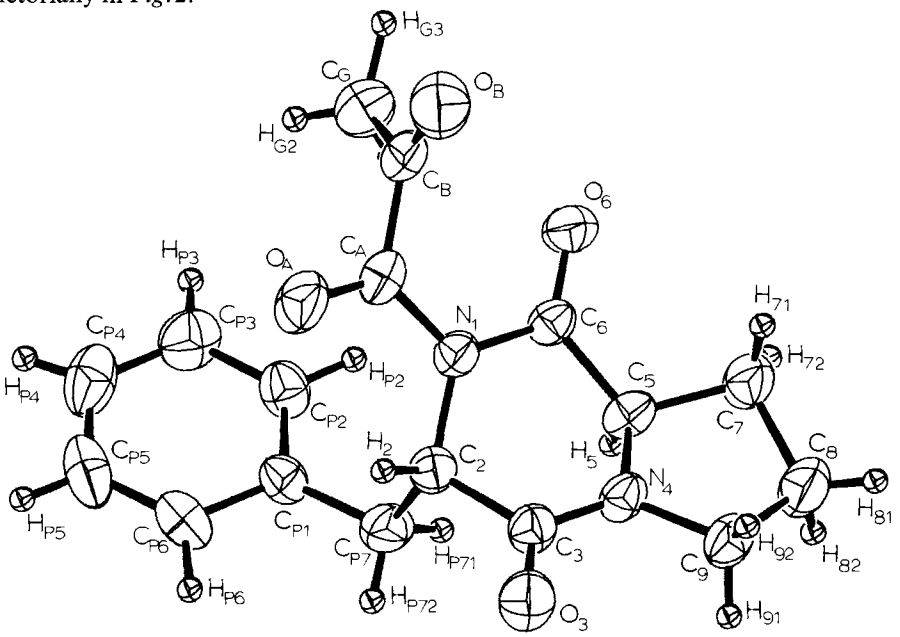


Fig. 1. *ORTEP diagram for pyroergotamine, showing numbering system used*

[3]) *The structures illustrated* in this paper refer to the cleavage product of dihydroergotamine.

Table 1. *Atomic Coordinates in Crystalline Pyroergotamine*[a])

Atom type[b])	*x*	*y*	*z*	Isotropic thermal parameter *B* [Å][c])
N(1)	0.8468(3)	0.4200	0.4071(2)	2.8
C(2)	1.0327(4)	0.3630(2)	0.5009(3)	3.0
C(3)	1.1198(4)	0.2979(2)	0.3986(3)	3.1
N(4)	0.9609(3)	0.2614(2)	0.2817(2)	2.9
C(5)	0.7207(4)	0.2804(2)	0.2530(3)	2.9
C(6)	0.6801(4)	0.3806(2)	0.2856(3)	2.8
C(7)	0.6236(5)	0.2518(3)	0.0841(4)	3.9
C(8)	0.7761(6)	0.1720(3)	0.0684(5)	4.5
C(9)	1.0074(5)	0.1992(3)	0.1667(3)	3.7
O(3)	1.3207(3)	0.2803(2)	0.4241(3)	4.1
O(6)	0.5189(3)	0.4238(2)	0.2136(3)	3.9
C(A)	0.8466(5)	0.5143(2)	0.4395(3)	3.2
O(A)	0.9935(4)	0.5507(2)	0.5391(3)	4.5
C(B)	0.6550(6)	0.5757(2)	0.3437(3)	3.6
O(B)	0.6923(6)	0.6203(2)	0.2412(3)	5.3
C(G)	0.4540(7)	0.5854(4)	0.4010(5)	5.1
C(P1)	0.8982(4)	0.3694(2)	0.7432(3)	3.0
C(P2)	0.6784(4)	0.4014(3)	0.7109(3)	3.5
C(P3)	0.6153(6)	0.4624(3)	0.8096(4)	4.4
C(P4)	0.7693(7)	0.4908(3)	0.9438(4)	4.4
C(P5)	0.9843(7)	0.4576(3)	0.9798(3)	4.2
C(P6)	1.0506(5)	0.3980(3)	0.8804(3)	3.7
C(P7)	0.9687(5)	0.3084(3)	0.6303(3)	3.7
H(2)	1.146(6)	0.404(3)	0.544(4)	2(1)
H(5)	0.660(5)	0.245(2)	0.318(4)	1(1)
H(P71)	0.846(6)	0.261(3)	0.586(4)	3(1)
H(P72)	1.097(6)	0.276(3)	0.685(4)	3(1)
H(P2)	0.567(7)	0.382(3)	0.615(5)	3(1)
H(P3)	0.472(7)	0.484(3)	0.788(5)	4(1)
H(P4)	0.737(7)	0.524(3)	1.018(5)	3(1)
H(P5)	1.075(7)	0.474(3)	1.071(3)	4(1)
H(P6)	1.210(7)	0.370(3)	0.897(4)	3(1)
H(71)	0.643(7)	0.304(3)	0.011(5)	3(1)
H(72)	0.473(6)	0.233(3)	0.069(4)	2(1)
H(81)	0.768(8)	0.155(4)	−0.032(6)	4(1)
H(82)	0.723(9)	0.115(4)	0.108(6)	5(1)
H(91)	1.092(7)	0.149(3)	0.215(5)	3(1)
H(92)	1.109(6)	0.231(3)	0.106(4)	2(1)
H(G1)	0.402(11)	0.520(5)	0.422(7)	7(1)
H(G2)	0.485(10)	0.605(4)	0.498(8)	5(1)
H(G3)	0.345(10)	0.631(4)	0.324(6)	6(1)

[a]) Figures in parentheses are the estimated standard deviations. [b]) Atoms labelled to agree with *Fig. 1*.
[c]) Isotropic thermal parameter calculated from $B = 4[V^2\det(\beta_{ij})]^{1/3}$.

Each of the two peptide linkages in the DKP ring is nearly planar. Atoms C(2), C(3), O(3), N(4), C(5), and C(9) are coplanar to within 0.02 Å while atoms N(1), C(2), C(A), C(5), C(6), and O(6) are coplanar to within 0.07 Å. The mean planes of these two peptide linkages intersect in a dihedral angle of 42° to form a DKP ring which is boat-shaped and folded along the C(2)···C(5) vector.

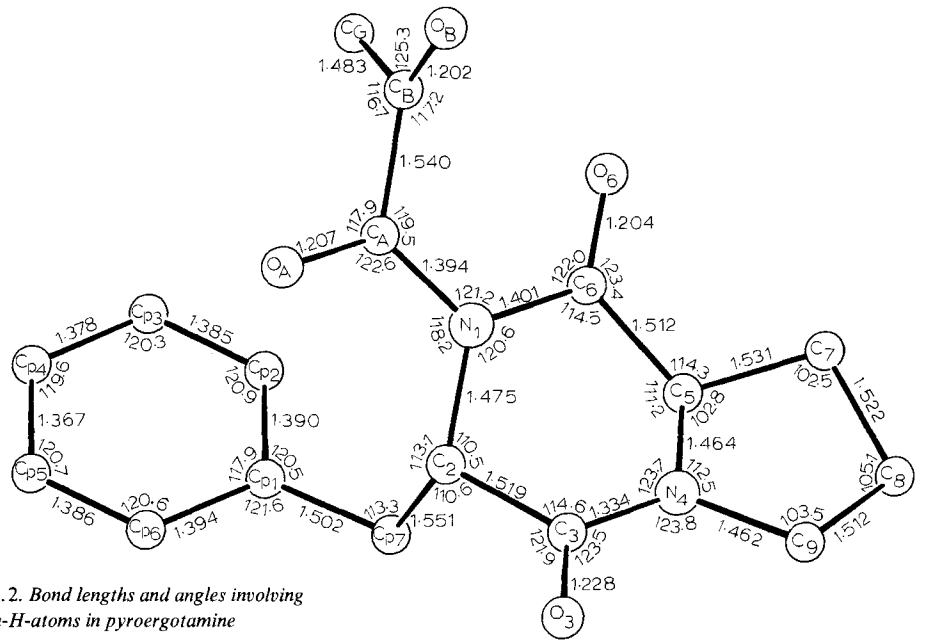


Fig. 2. *Bond lengths and angles involving non-H-atoms in pyroergotamine*

The pyrrolidine ring has an envelope conformation and is folded by 36° about the C(5)···C(8) vector. N(4), C(5), C(8), and C(9) are coplanar to within 0.03 Å, and C(7) is displaced from their mean plane by 0.56 Å in the same direction as O(6). The small 0.10 Å displacement of C(8) from the 6-atom C(3)–N(4) peptide linkage indicates a nearly coplanar arrangement for this peptide and the planar portion of the pyrrolidine ring.

The conformation of the rest of the molecule is largely dictated by the near coplanarity of atoms O(A) and C(B) with the N(1)–C(6) peptide linkage. Atoms N(1), C(2), C(5), C(6), O(6), C(A), O(A), and C(B) are coplanar to within 0.11 Å *(Fig. 3)*. This coplanarity is presumably due to the delocalization of π electrons over the amide links of the molecule which increases the N(1)–C(6) bond length and decreases the C(6)–O(6) bond length relative to the expected values for a simple peptide linkage [10a]. The N(1)–C(A) bond length is also shorter than would be expected for a pure single bond, indicating partial double bond character. The coplanarity of these atoms forces C(B) into close proximity with O(6), and O(A) into close proximity with H_2 *(Fig. 3)*. Further crowding in this region of the molecule is reduced by an 87° rotation of the acyl group (C(G), C(B), O(B)) about the C(A)–C(B) bond out of the plane for the 8-atom grouping containing the N(1)–C(6) peptide linkage. One striking feature of the solid-state conformation *(Fig. 3)* is that H-atom H(2) is sandwiched between O-atoms O(A) and O(3) with H···O contacts that are 0.29 Å and 0.11 Å smaller than the *van der Waal*'s contact distance of 2.60 Å [10b].

The benzyl residue is pseudo-axial to the boat-shaped DKP ring. The greater stability of *trans*-isomers of *cyclo*(Pro-Ala) relative to the *cis*-isomers is the result of unfavourable contacts for the alanine R group in the pseudo-equatorial position where it eclipses the adjacent C = O and N–H bonds [11]. In **1**, these effects would be larger since the N-atom is acylated. The fact that the pyrolysis of the dihydro alkaloid **2** is accompanied by

Table 2. *Bond Lengths and Angles Involving Non-H-Atoms in Crystalline Pyroergotamine*[a])

Parameter[b])	Value	Parameter[b])	Value
		Bond Lengths [Å]	
N(1)–C(2)	1.475(3)	C(2)–C(3)	1.519(4)
N(4)–C(5)	1.464(3)	C(5)–C(6)	1.512(3)
N(4)–C(9)	1.462(3)	C(P1)–C(P7)	1.502(4)
N(1)–C(A)	1.394(4)	C(2)–C(P7)	1.551(4)
N(1)–C(6)	1.401(3)		
		C(5)–C(7)	1.531(4)
N(4)–C(3)	1.334(3)	C(7)–C(8)	1.522(4)
		C(8)–C(9)	1.512(5)
C(3)–O(3)	1.228(3)		
		C(P1)–C(P2)	1.390(4)
C(6)–O(6)	1.204(3)	C(P1)–C(P6)	1.394(5)
C(A)–O(A)	1.207(4)	C(P2)–C(P3)	1.385(4)
C(B)–O(B)	1.202(4)	C(P3)–C(P4)	1.378(5)
		C(P4)–C(P5)	1.367(6)
C(A)–C(B)	1.540(4)	C(P5)–C(P6)	1.386(5)
C(B)–C(G)	1.483(5)		
		Bond Angles [deg]	
C(A)–N(1)–C(2)	118.2(2)	C(P6)–C(P1)–C(P2)	117.9(3)
C(A)–N(1)–C(6)	121.2(2)	C(P1)–C(P2)–C(P3)	120.9(3)
C(2)–N(1)–C(6)	120.6(2)	C(P2)–C(P3)–C(P4)	120.3(3)
C(3)–N(4)–C(5)	123.7(2)	C(P3)–C(P4)–C(P5)	119.6(3)
C(3)–N(4)–C(9)	123.8(2)	C(P4)–C(P5)–C(P6)	120.7(3)
C(5)–N(4)–C(9)	112.5(2)	C(P5)–C(P6)–C(P1)	120.6(3)
		C(P2)–C(P1)–C(P7)	120.5(2)
O(A)–C(A)–N(1)	122.6(3)	C(P6)–C(P1)–C(P7)	121.6(3)
O(A)–C(A)–C(B)	117.9(2)		
N(1)–C(A)–C(B)	119.5(2)	N(1)–C(2)–C(3)	110.5(2)
O(B)–C(B)–C(A)	117.2(3)	N(1)–C(2)–C(P7)	113.1(2)
O(B)–C(B)–C(G)	125.3(3)	C(3)–C(2)–C(P7)	110.6(2)
C(A)–C(B)–C(G)	116.7(3)	N(4)–C(5)–C(6)	111.2(2)
O(3)–C(3)–N(4)	123.5(2)	N(4)–C(5)–C(7)	102.8(2)
O(3)–C(3)–C(2)	121.9(2)	C(6)–C(5)–C(7)	114.3(2)
N(4)–C(3)–C(2)	114.6(2)	C(5)–C(7)–C(8)	102.5(2)
O(6)–C(6)–N(1)	122.0(2)	C(7)–C(8)–C(9)	105.1(2)
O(6)–C(6)–C(5)	123.4(2)	N(4)–C(9)–C(8)	103.5(2)
N(1)–C(6)–C(5)	114.5(2)	C(2)–C(P7)–C(P1)	113.3(2)

[a]) Figures in parentheses are the estimated standard deviations in the last significant digit.
[b]) Atoms are labelled in agreement with *Fig. 1*.

inversion ((*S*) to (*R*)) in the proline residue [1] [4] rather than the phenylalanine suggests that the mechanism of the pyrolysis involves the proton loss shown in **2**. The benzyl group exists in the conformation in which the phenyl group is extended to N (**7a**) [12a].

Examination of the dihedral angles of type one (*Table 3*) show that the conformations of *cyclo*((*S*)-Pro-(*S*)-Leu) [13] *cyclo*((*S*)-Pro-(*S*)-Pro) [14] and *cyclo*((*S*)-Pro-Gly) [15] (as determined by X-ray crystallography) are very similar to that of **1**. The DKP's are boats and the pyrrolidines are envelopes with C(β) (C(7) in **1**) out of plane. By contrast the conformation of *cyclo*((*S*)-Pro-(*R*)-Phe) in the solid state [16] is not the same as that of **1**: the DKP ring is a shallow boat with different dihedral angles (*Table 3*); the pyrrolidine is not an envelope and has atoms C(α) and C(β) above a plane defined by N,

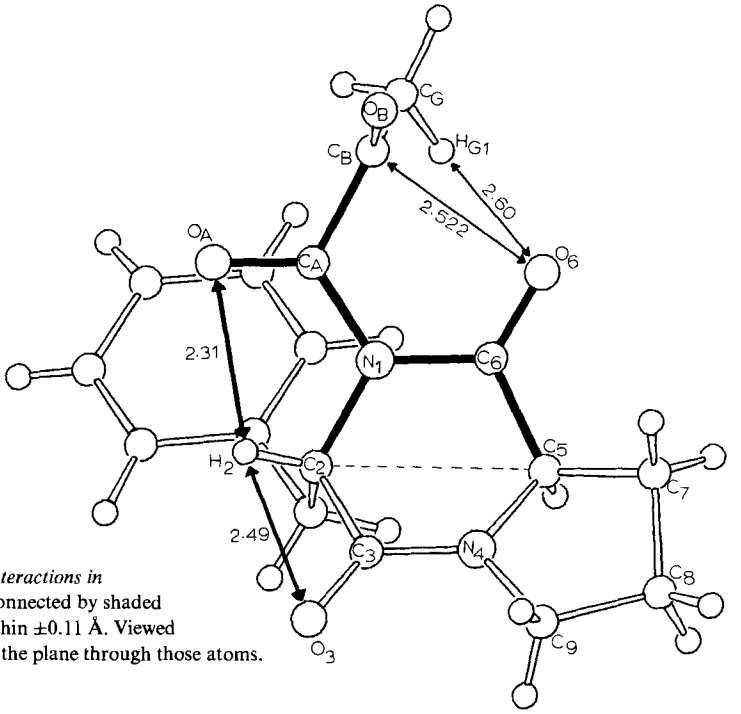
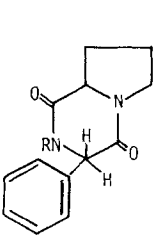
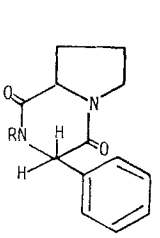


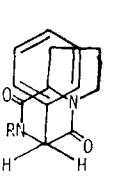
Fig. 3. *Some nonbonded interactions in pyroergotamine.* Atoms connected by shaded bonds are coplanar to within ±0.11 Å. Viewed approximately normal to the plane through those atoms.



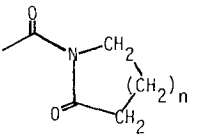
7a Extended to N



7b Extended to O



7c Folded



8 (*E,Z*)

C(γ), and C(δ); and finally the benzyl group is in the folded conformation with the phenyl above the plane of the ring (**7c**). Theoretical studies [17] have shown that folding the phenyl group over the DKP leads to a flattening of the boat. The enthalpy of the folded conformation in *cyclo*((*S*)-Pro-(*R*)-Phe) is about 3 kcal/mol less than that of the extended conformations. Perhaps an interaction between the phenyl and the N(1)C(A)O(A) amide in **1** is responsible for stabilising the N-extended conformation in **1**.

Conformation in Solution. The conformation of DKP's in solution were first studied experimentally by *Kopple* and *Marr* [18], *Kenner et al.* [19], and *Blaha* and *Samek* [20], and theoretically by *Caillet* and *Pullman* [21], and *Chandrasekaram et al.* [22]. *Kopple*'s work on monocyclic DKP's containing tyrosine shows that the enthalpy and entropy of the folded form are both less than those of the extended, and hence the free energy differences between the forms are small [18b]. Particular attention has been paid to DKP's contain-

Table 3. *Dihedral Angles (°) of Type* **1** *in Pyroergotamine and Related Cyclopropyl-DKP's*[a])[b])

Dihedral	Atoms Involved	A[c])	B	C	D	E
ϕ_1	C(3)–N(4)–C(5)–C(6)	38.5	−41.5	−38	−44	−17.1
ψ_1	N(1)–C(6)–C(5)–N(4)	−34	33.7	37	38.5	14.9
ω_1	C(2)–N(1)–C(6)–C(5)	−5.2	6.3	0.7	0.4	2.8
ϕ_2	C(3)–C(2)–N(1)–C(6)	42.3	−41.5	−37	−37.3	−19
ψ_2	N(1)–C(2)–C(3)–N(4)	−38.8	33.8	36	32.7	16.6
ω_2	C(2)–C(3)–N(4)–C(5)	−0.8	6.2	−0.7	7.4	0.7
χ_1^1	N(4)–C(5)–C(7)–C(8)	32.8	−31.5	−32	−32.7	−37.9
χ_1^2	C(5)–C(7)–C(8)–C(9)	−36.8	36.0	36	35.6	31.9
χ_1^3	C(7)–C(8)–C(9)–N(4)	26	−25.1	−24	−24	−13.5
χ_1^4	C(8)–C(9)–N(4)–C(5)	−5	4.5	3	3.2	−11.3
χ_2^1	N(1)–C(2)–C(P7)–C(P1)	−59.9	−72.3	–	–	−75.0

[a]) *Cf. Table 6* in [16].

[b]) A: Pyroergotamine; B: *cyclo*((*S*)-Pro-(*S*)-Leu) [13]; C: *cyclo*((*S*)-Pro-(*S*)-Pro) [14]; D: *cyclo*((*S*)-Pro-Gly) [15]; E: *cyclo*((*S*)-Pro-(*R*)-Phe) [16].

[c]) The signs in column A should be inverted to facilitate the comparison of the conformation of A with those of B–E. This is because: *i*) A and E have enantiomeric DKP's; *ii*) epimerisation of C(5) in A causes the bow and stern of the boat (C(2) and C(5)) to flip through the plane N(1)–C(6)–N(4)–C(3).

ing proline. These compounds, which are more rigid than monocyclic DKP's, have been investigated using physical (^{1}H- and ^{13}C-NMR, CD and IR [12] [23–25]) and theoretical [17] methods. Where direct comparison is possible the conformations in solution and the solid state are similar. There is general agreement from experimental and theoretical studies that the *cis*- and *trans-cyclo*(Pro-Phe) DKP's have different conformations in solution: the *cis*-compound exists as a boat with the phenyl group in the N-extended conformation; the *trans*-compound as a flattened boat with the phenyl in a folded conformation. A striking result of the presence of the folded conformation is that the phenyl group has a significant shielding effect on the C proline *cis* to it; *e.g.*, the signal for H–C(α) in proline is at 4.07 ppm in *cis*- and 2.90 ppm in *trans-cyclo*(Pro-Phe) [23].

The H–C(5) signal in **1** appears at 2.3 ppm (in $CDCl_3$) and 3.1 ppm (in CD_3COCD_3). These data indicate that the phenyl group is mainly in the folded conformation in $CDCl_3$, and to a much lesser extent in acetone[4]). A folded conformation is associated with a flattened DKP ring. The difference of 6.7 ppm, which we observe in the ^{13}C shifts of C(7) and C(8) (C(β) and C(γ) in the proline residue), indicates that the DKP ring is mainly in the planar form [25b]. The predominance of the folded conformation in solution, rather than the N-extended form as in the solid state differs from the results with *trans-cyclo*-(Pro-Phe) in which the flattened boat-folded conformation predominates both in solution and the solid state. As the differences between the free energies of the rotamers are small (1–2 kcal/mol), it is not easy to explain why the conformation of **1** (an *N*-acyl-DKP) differs so much from its parent DKP in the solid state but not in solution.

The preferred conformation for *N*-acyl-lactams in solution is the (*E*,*Z*) (**8**) [26]. This is also the conformation of **1** in the solid state. Even with some flattening of the ring induced through the folding of the phenyl group, the steric relationships of H–C(2), O(A), and O(3) observed in the solid state should also be present in solution. We account for the

[4]) The solvent effect is surprising, *cf.* [12a].

NMR signal for H–C(2) at lower than expected fields as being due to deshielding effects of the carbonyl groups which are squeezed against the hydrogen[5]).

Several other conformations should be possible and are populated in solution. The most important involve rotations about the C(A)–C(B), C(A)–N(1), and C(P1)–C(P7) bonds. The largest barrier to rotation should be in the C(A)–N(1) bond which is frozen out at low temperature thus leading to a splitting of the CH_3 signal in the ^{1}H-NMR into a doublet. Although the two peaks are not sufficiently resolved to enable us to determine accurately the height of the barrier to rotation, the coalescence temperatures for this change and the k_r's determined in CD_2Cl_2 and CD_3COCD_3 are consistent with those determined by *Noe* and *Raban* for open-chain imides [26]. Slowing of the rotation about the C(A)–N(1) bond would also account for the broadening at low temperatures of the ^{13}C signal for C(2).

Finally, the resistance of the ketone group to hydrogenation deserves comment. The planarity imposed by the imide system leaves the C(B)–O(6) distance at 2.55 Å. The positions of the ^{13}C peaks for the ketone (192 ppm) and CH_3 (25.6 ppm) groups in $CDCl_3$ are not sufficiently different from those of the corresponding peaks in pyruvamide (197 and 24.5 in DMSO) to suggest any special electronic interaction between the C(B) and O(6). However, the distance itself is short enough to hinder the transformation of C(B) from sp^2 to sp^3; this presumably accounts for the failure of pyroergotamine to undergo catalytic reduction.

Experimental Part

Pyroergotamine, $C_{17}H_{18}N_2O_4$, after crystallisation from MeOH had m.p. 183°. ^{1}H-NMR (100 MHz, $CDCl_3$)[6]): 7.0–7.5 (*m*, 5 arom. H); 5.1 (*t*, *J* = 4, H–C(2)); 3.0–3.7 (*m*, 2H–C(9), 2H–C(P7)); 2.4 (*s*, $COCH_3$); 2.2–2.4 (*m*, H–C(5)); 1.4–2.15 (*m*, 2H–C(7), 2H–C(8)). The ^{1}H assignments were confirmed by decoupling experiments. The ^{1}H-NMR spectra in CD_2Cl_2 and ^{1}H- and ^{13}C-NMR in CD_3COCD_3 are very similar to those in $CDCl_3$, except that the H–C(5) peak was shifted to 3.1 in CD_3COCD_3. ^{13}C-NMR (25.2 MHz, $CDCl_3$)[7]): 192.2 (C(B)); 169.3 (C(3) or C(6)); 168.3 (C(6) or C(3)); 162.8 (C(A)); 134.4 (C(P1)); 129.7 (C(P2) and C(P6)); 128.4 (C(P3) and C(P5)); 127.5 (C(P4)); 59.3 (C(2)); 57.6 (C(5)); 44.9 (C(9)); 37.3 (C(P7)); 28.4 (C(7)); 25.6 (C(6)); 21.7 (C(8)).

Variable-Temperature Studies. ^{1}H-NMR spectra in CD_3COCD_3 and CD_2Cl_2 were measured at 5° intervals from −50° to −90°. In both solvents the main change was the splitting of the CH_3 peak into a doublet: in CD_3COCD_3 the coalescence temperature was −67° ± 3° and the splitting was 9 Hz ($k_r = 20$); in CD_2Cl_2 the coalescences was at 72° ± 3° and the splitting 5.5 Hz ($k_r = 12$).

The ^{13}C-NMR spectrum was measured in CD_3COCD_3 at −95° and in $CDCl_3$ at −60°. The only significant change from the spectra at r.t. was a broadening in the peak corresponding to C(2).

X-Ray Analysis[8]). Large well-shaped single crystals of pyroergotamine ($C_{17}H_{18}N_2O_4$, mol.-wt. 314) suitable for X-ray diffraction studies were grown from MeOH. They are mono clinic, space groups P_{2_1}–C_2^2 (No. 4) [28] with a = 6.197(1) Å, b = 14.458(4) Å, c = 9.025(2) Å, β = 106.24(2) Å, and Z = 2 at 20 ± 1 °C [$d_{calc.}$ = 1.345 g cm^{-3}, $d_{measd.}$ = 1.336 g cm^{-3}, $\mu_a(MoK_\alpha)^R$ = 0.10 mm^{-1}]. Intensity measurements were made on a *Syntex P1* autodiffrac-

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[5]) As the H–C(2) signal appears in the same place in both $CDCl_3$ and CD_3COCD_3, it is clearly not affected by the degree to which the folded conformation is preferred. Examination of models also suggests that flattening the DKP ring will not change greatly the O(A)–H(2)–O(3) distances.

[6]) NMR spectra measured on a *Varian* spectrometer, with chemical shift (δ) reported in ppm downfield from TMS.

[7]) The assignments of the signals for the C-atoms parallel those reported for the corresponding C-atoms in ergotamine [27].

[8]) Supplementary material is available in the *Crystallographic Data Centre, Cambridge (U.K.)*.

tometer for a nearly cube-shaped specimen (0.50 × 0.62 × 0.62 mm) which was glued to the end of a glass fiber with a tip diameter of 0.10 mm. A total of 3677 independent reflections having $2\theta_{MoK_\alpha} < 71°$ (twice the number of data in the limiting CuK_α sphere) were collected using θ–2θ scans and Nb-filtered MoK_α radiation. A scanning rate of 3°/min was employed for the scan between 2θ settings 1.0° above and below the calculated K_α doublet values ($\lambda_{K_{\alpha 1}} = 0.70926$ Å and $\lambda_{K_{\alpha 2}} = 0.71354$ Å) of each reflection. Background counts, each lasting for half the total scan time were taken at both ends of the scan range.

The 23 non-H-atoms comprising the asymmetric unit appeared simultaneously on an E map which was calculated from a trial set of statistical direct methods (MULTAN) phases. All 18 chemically-anticipated H-atoms were located from a difference *Fourier* synthesis calculated from a full-matrix least-squares refined structural model [R_1 (unweighted, based on F) = 0.084, R_2 (weighted, based on F) = 0.079 for 2193 reflections having $2\theta_{Mo_\alpha} < 71°$ and $I > 3\sigma(I)$] which incorporated unit weighting and anisotropic thermal parameters for all non-H-atoms. All structure factor calculations employed the atomic form-factors compiled by *Cromer* and *Mann* [29]. The final cycles of empirically-weighted[9]) full-matrix least-squares refinement which employed isotropic thermal parameters for H-atoms and anisotropic thermal parameters for all others, converged to values of 0.046 and 0.05 for R_1 and R_2, respectively, for 2193 independent reflections having $2\theta_{MoK_\alpha} < 71°$ and $I > 3\sigma(I)$[8]). Since a careful comparison of F_0 and F_c values indicated the absence of extinction effects, no extinction corrections were applied.

We are grateful to Drs. *M. Raban, W.E. Waghorne, C.A. Kingsbury, A. von Wartburg,* and *P. Pfäffli* for helpful comments. *D.M.S.W.* thanks Drs. *A. Sopchik* and *T.D. Brunner* for the NMR spectra.

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[9]) For empirical weights: $\sigma_F = \sum_0^3 a_n|F_o|^n = a_o + a_1|F_o| + a_2|F_o|^2 + a_3|F_o|^3$, the a_n being coefficients from the least-squares fitting of the curve $||F_o| - |F_c|| = \sum_0^3 a_n|F_o|^n$. In this case: $a_o = 0.201$, $a_1 = 5.47 \times 10^{-3}$, $a_2 = 5.33 \times 10^{-4}$, $a_3 = -3.60 \times 10^{-6}$.

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