The Normal Vibrations of Diketopiperazine and Its N-Deuterated Compound

By Kunio FUKUSHIMA, Yoshiko IDEGUCHI and Tatsuo MIYAZAWA

(Received October 21, 1963)

The infrared absorption bands of the *trans*-CONH group have been extensively studied.[1] On the other hand, the characteristic vibrations of the *cis*-CONH group have not been established. Newman and Badger[2] and Shimanouchi et al.[3] measured the infrared dichroism of single crystals of diketopiperazine in the region above 700 cm^{-1} and assigned the observed bands to the A_1 or B_u fundamental vibrations. Miyazawa, measuring the infrared spectra of diketopiperazine and its *N*-deuterated compound, assigned that absorption bands with reference to the isotope shifts and to the normal vibration calculation for the planar cis form of *N*-methylacetamide.[4]

In the present study the normal vibrations (B_u) of diketopiperazine and its *N*-deuterated compound are treated, and the origin of the infrared bands is studied. The nature of the characteristic vibrations of the *cis*-CONH group will also be elucidated.

Normal Coordinate Treatment

According to the X-ray diffraction study by Corey,[5] the molecule of diketopiperazine is planar (except for the hydrogen atoms of the methylene groups) with the point group, C_{2h}. On the basis of this model, we have calculated the normal vibrations of diketopiperazine and its *N*-deuterated compound as a ten-body problem, treating the methylene groups as mass points. Wilson's ***GF*** matrix method[6] was used for the calculation. The internal coordinates are as shown in Table I, while the molecular parameters used are the same as those of polyglycine I.[7] The inverse kinetic energy matrix, $\boldsymbol{G}(B_u)$, for the B_u vibrations was constructed in terms of the symmetry coordinates:

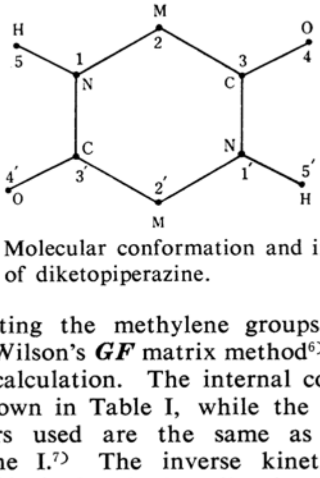

Fig. 1. Molecular conformation and indices of atoms of diketopiperazine.

$$S_j = (R_i - R_i')/2^{1/2} \quad (i=1, 2, \cdots\cdots, 10) \quad (1)$$

The two redundant coordinates were removed by the numerical diagonalization of the ***G*** matrix. The potential energy matrix, $\boldsymbol{F}(B_u)$, was derived from the Urey-Bradley potential function,[8] and the potential constants were taken to be the same as those of polyglycine I.[7] The numerical computations were made with an NEAC 2101 electronic computer. The calculated frequencies, the diagonal terms of the potential energy distributions, and the atomic displacements are shown in Tables II and III, and Figs. 2 and 3, respectively.

---

[1] T. Miyazawa, *Kagaku to Kogyo*, **15**, 137 (1962); "Polyamino-acids, Polypeptides, and Proteins," Ed. by M. Stahmann, University of Wisconsin Press, Madison (1962), p. 201.

[2] R. Newman and R. M. Badger, *J. Chem. Phys.*, **19**, 1147 (1951).

[3] T. Shimanouchi, K. Kuratani and S. Mizushima, ibid., **19**, 1479 (1951).

[4] T. Miyazawa, *J. Mol. Spectr.*, **4**, 155 (1960).

[5] R. B. Corey, *J. Am. Chem. Soc.*, **60**, 1598 (1938).

[6] E. B. Wilson, Jr., *J. Chem. Phys.*, **7**, 1047 (1939); **9**, 76, (1941).

[7] K. Fukushima, Y. Ideguchi and T. Miyazawa, This Bulletin, **36**, 1301 (1963).

[8] T. Shimanouchi, *J. Chem. Phys.*, **17**, 245 (1949).

TABLE I. INTERNAL COORDINATES

R_1	Δr_{15}	$R_{1'}$	$\Delta r_{1'5'}$
R_2	$\Delta(2\alpha_{3'12}-\alpha_{513'}-\alpha_{215})/6^{1/2}$	$R_{2'}$	$\Delta(2\alpha_{31'2'}-\alpha_{5'1'3}-\alpha_{2'1'5'})/6^{1/2}$
R_3	$\Delta(\alpha_{513'}-\alpha_{215})/2^{1/2}$	$R_{3'}$	$\Delta(\alpha_{5'1'3}-\alpha_{2'1'5'})/2^{1/2}$
R_4	Δr_{12}	$R_{4'}$	$\Delta r_{1'2'}$
R_5	$\Delta\alpha_{123}$	$R_{5'}$	$\Delta\alpha_{1'2'3'}$
R_6	Δr_{23}	$R_{6'}$	$\Delta r_{2'3'}$
R_7	Δr_{34}	$R_{7'}$	$\Delta r_{3'4'}$
R_8	$\Delta(2\alpha_{231'}-\alpha_{432}-\alpha_{1'34})/6^{1/2}$	$R_{8'}$	$\Delta(2\alpha_{2'3'1}-\alpha_{4'3'2'}-\alpha_{13'4'})/6^{1/2}$
R_9	$\Delta(\alpha_{432}-\alpha_{1'34})/2^{1/2}$	$R_{9'}$	$\Delta(\alpha_{4'3'2'}-\alpha_{13'4'})/2^{1/2}$
R_{10}	$\Delta r_{31'}$	$R_{10'}$	$\Delta r_{3'1}$

TABLE II. THE DIAGONAL TERMS OF POTENTIAL ENERGY DISTRIBUTIONS (IN %)

(-CH_2CONH-)$_2$

ν_c	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}
3339	101	0	0	0	0	0	0	0	0	0
1657	0	1	16	1	0	3	70	9	0	18
1450	0	0	80	3	1	0	18	0	1	0
1383	0	2	0	6	0	25	4	0	13	72
1056	0	9	2	68	0	2	0	1	17	2
892	0	4	3	0	7	61	2	0	10	10
728	0	22	1	7	19	0	9	40	0	1
403	0	2	0	15	1	11	1	1	65	1

(-CH_2COND-)$_2$

ν_c	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}
2437	101	0	0	0	0	0	0	0	0	0
1639	0	1	4	0	1	3	81	9	0	19
1381	0	2	2	9	0	23	7	0	11	70
1195	0	1	54	20	1	8	5	1	15	0
1010	0	9	12	47	0	17	2	0	5	6
812	0	3	25	4	8	38	0	0	11	6
720	0	21	5	5	16	1	9	40	0	1
401	0	2	0	16	1	11	1	2	64	1

TABLE III. OBSERVED (ν_o) AND CALCULATED (ν_c) FREQUENCIES (IN cm^{-1}) OF DIKETOPIPERAZINE AND ITS *N*-DEUTERATED COMPOUND AND THEIR ASSIGNMENTS

(-CH_2CONH-)$_2$		(-CH_2COND-)$_2$		Assignment
ν_o	ν_c	ν_o	ν_c	
1690	1657	1675	1639	C=O stretch.
1443	1450			N-H in-plane bend.
1340	1383	1349	1381	C-N stretch., C-CH_2 stretch.
		1232	1195	N-D in-plane bend., N-CH_2 stretch.
1075	1056			N-CH_2 stretch., C=O in-plane bend.
		970	1010	N-CH_2 stretch., C-CH_2 stretch., N-D in-plane bend.
910	892			C-CH_2 stretch., C-N stretch., C=O in-plane bend.
		887	812	C-CH_2 stretch., N-D in-plane bend.
806	728	780	720	CH_2-C-N deform., C-N-CH_2 deform.
449	403	446	401	C=O in-plane bend., N-CH_2 stretch.

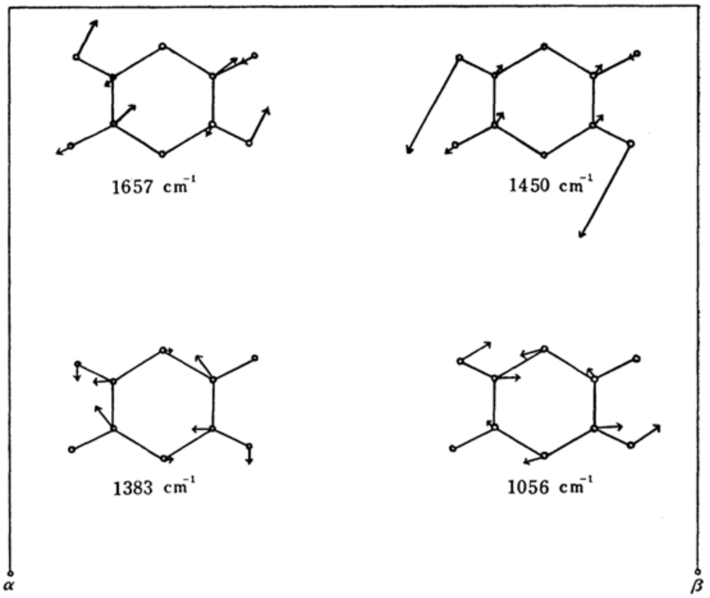

Fig. 2a.

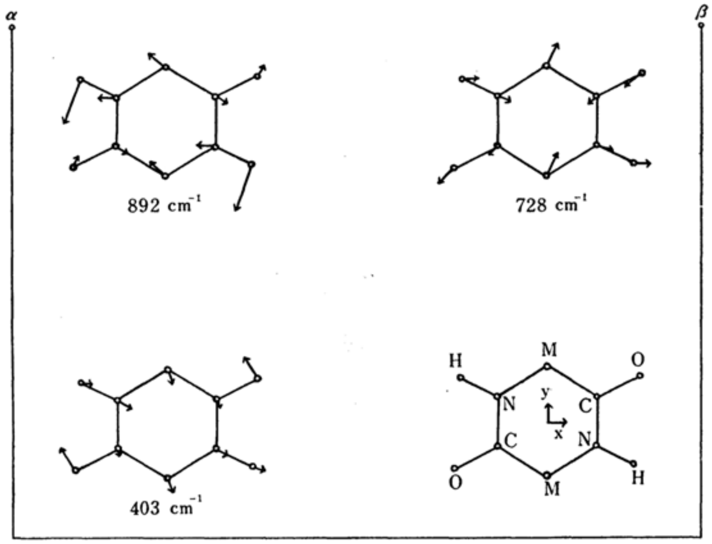

Fig. 2b.

Fig. 2. Schematic representation of the vibrational modes of diketopiperazine.

Assignments

With reference to the calculated frequencies and the potential energy distributions, the observed infrared bands[4)] may be assigned as shown in Table III. The present assignment agrees with the previous assignments except for the few cases described below (the abbreviations DP and DP-d represent diketopiperazine and *N*-deuterated diketopiperazine respectively). The band of DP at 806 cm^{-1} has been established as due to B_u vibrations.[2,3)] In a previous study[4)] this band has been assigned to the C=O in-plane bending mode. However, since the observed frequency corresponds most closely with the calculated frequency at 728 cm^{-1}, this band is now assigned to the ring deformation vibration. The dichroism of the bands at 449 cm^{-1} (DP) and at 446 cm^{-1} (DP-d) have not been determined experimentally. These bands correspond to the B_u frequency calculated at 403 cm^{-1} (DP) and at 401 cm^{-1} (DP-d) respectively, and are now assigned to the C=O in-plane bending mode as coupled slightly with the N–CH_2 stretching mode.

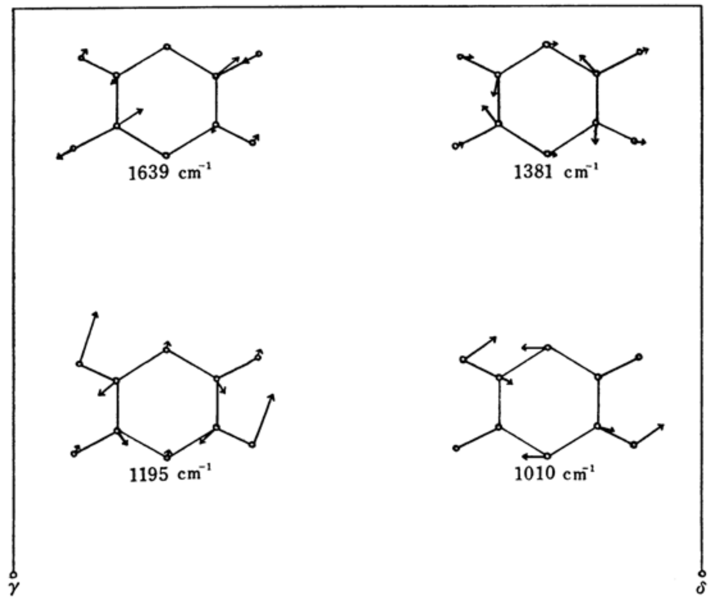

Fig. 3a.

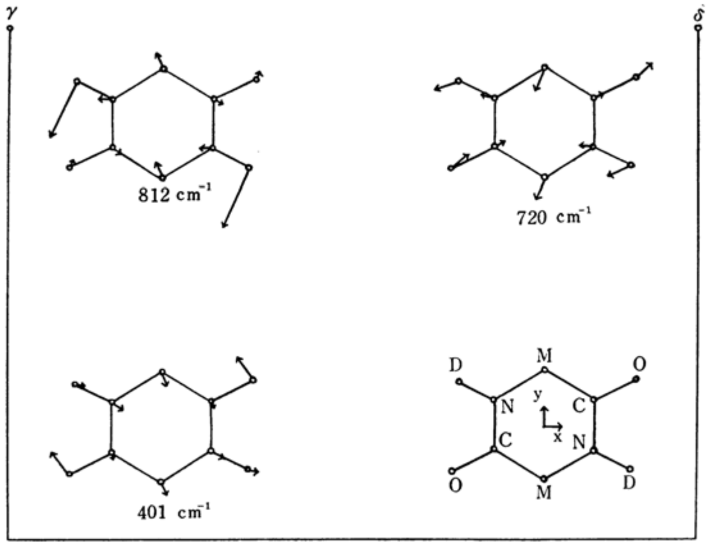

Fig. 3b.

Fig. 3. Schematic representation of the vibrational modes of *N*-deuterated diketopiperazine.

The Characteristic Vibrations of the *cis*-CONH Group

The *cis*-Amide I Band (C=O Stretching Vibration).—For this vibration at 1690 cm^{-1}, 70% of the potential energy is associated with the C=O stretching mode. However, the energy distributions at the C–N stretching (18%) and the N–H bending modes (16%) are not quite negligible.

The *cis*-Amide II Band (N–H In-plane Bending Vibration). — For this vibration at 1443 cm^{-1}, 80% of the potential energy is associated with the N–H in-plane bending mode, while 20% of the energy is associated with the C=O stretching mode.

The *cis*-Amide III Band (C–N Stretching Vibration).—For this vibration at 1340 cm^{-1}, 70% of the potential energy is associated with the C–N stretching mode, and 25% of the energy is associated with the C–CH_2 stretching mode.

The *cis*-Amide IV Band (C=O In-plane Bending Mode).—For this vibration at 449 cm^{-1}, 65% of the potential energy is associated with the C=O in-plane bending mode, while 26% of the energy is associated with the N-CH_2-C symmetric streching mode. This vibration is not localized in the CONH group as highly as are the *cis*-amide I, II, or III vibrations.

The *N*-Deuterated *cis*-Amide Group.—On *N*-deuteration, the frequencies and the potential energy distributions of the *cis*-amide I, III, or IV vibrations do not change appreciably (Tables II and III). The *cis*-amide II vibration is shifted to a much lower frequency, and then the N–D in-plane bending mode is strongly coupled with the C–N and C–C stretching modes (see Table III for the nature of the vibrations at 1195 cm^{-1} and 812 cm^{-1}).

Summary

The normal vibrations of diketopiperazine and its *N*-deuterated compound have been calculated, with the metylene groups treated as mass points. An assignment of the infrared absorption bands has been made on the basis of the calculated frequencies and potential energy distributions, and the nature of the characteristic vibrations of the *cis*-amide group has been discussed.

Institute for Protein Research
Osaka University
Kita-ku, Osaka