delocalization to the 1 position (alternatively, it has been suggested that the different dipolar orientation may be responsible).[23] However, in comparison with the rate of the parent compound, 1-methoxy substitution produced practically no rate enhancement (a factor of 1.2 at 25°) for *exo* solvolysis. This means that the +R carbonium ion stabilizing ability of the methoxy group has just overcome its large −I inductive effect.[24]

We conclude that methoxy groups have serious limitations as probes for charge delocalization in carbonium ions, *especially in saturated systems*. When little p character is developed at the methoxy-bearing carbon in the transition state resonance involving the oxygen lone pair electrons is not very effective, and the adverse inductive effect of the methoxy substituent may dominate the situation.[25] In such saturated systems, methyl groups (+R *and* +I) may be more effective. A different situation exists when methoxy is attached to a carbon (unsaturated or cyclopropanoid) with a large amount of p character. In such cases developing positive charge is transmitted relatively efficiently to oxygen, the +R effect dominates, and large rate enhancements are observed.[4–7]

Acknowledgments. This research was supported by grants from the National Science Foundation, the National Institutes of Health (AI 07766), and the Petroleum Research Fund, administered by the American Chemical Society.

[23] Reference 20, footnote 11.

[24] *Cf.* F. R. Jensen and B. E. Smart, *J. Amer. Chem. Soc.*, **91**, 5688 (1969).

[25] For an additional recent example, see I. Lillien and L. Handloser, *Tetrahedron Lett.*, 1213 (1970).

[26] National Institutes of Health Postdoctoral Fellows: (a) 1967–1968; (b) 1968–1970.

P. v. R. Schleyer, P. J. Stang,[26a] D. J. Raber[26b]
Department of Chemistry, Princeton University
Princeton, New Jersey 08540
Received April 20, 1970

Atomic Coordinates of Optically Active Pyrrolid-2-ones

Sir:

Owing to the importance of substituted pyrrolid-2-one molecular systems as models for optical rotation studies on the peptide chromophore,[1–8] we have initiated a program of determining the crystal structures of a series of these compounds. In the present communication we report the atomic coordinates for L-5-iodomethylpyrrolid-2-one and L-pyrrolid-2-one-5-carboxamide. These coordinates are the first to appear for pyrrolid-2-ones. They are particularly significant for optical rotation studies because of the high,[2–4] and perhaps even extreme,[6] sensitivity of calculated rotational strengths to the atomic parameters of moieties near the acyl portion of the peptide. A small but consistent nonplanarity, which should not be neglected for members of the molecular series with low rotational strength, such as the L-3-aminopyrrolid-2-one,[1,2,5,6] has been found. Furthermore, it has recently been suggested that the sign of the rotational strength of the peptide n–π* transition in lactams depends on the skeletal geometry and not on the peripheral molecular asymmetry.[9] The results, reported here, demonstrate that this is not the case, since both lactams have the same chiral sense or skeletal geometry but have large and oppositely signed rotational strengths (-35×10^{-40} for L-5-iodomethylpyrrolid-2-one and $+9.4 \times 10^{-40}$ for L-pyrrolid-2-one-5-carboxamide).[10] In addition these results confirm the absolute configuration of the series of pyrrolid-2-ones[2] derived initially from cyclization of glutamic acid.

L-5-Iodomethylpyrrolid-2-one crystallizes in the space group $P2_12_12_1$ with four molecules in the unit cell of a = 10.45 (1), b = 9.64 (1), c = 6.929 (7) Å. A crystal 0.5 × 0.2 × 0.1 mm was mounted along the needle axis on a Pailred diffractometer. For layers 0–7, 943 intensities above background were collected with Mo Kα radiation and a quartz monochromator. No correction for absorption was included. The structure was solved by Patterson and Fourier methods. Application of the R-factor ratio test[11] indicated the absolute configuration with a probable error of less than 0.5%. After six peaks at reasonable locations for hydrogen atoms appeared on a difference map (the hydrogens attached to C_1 did not appear), all hydrogen atoms were assigned tetrahedral positions 1.08 Å from the carbon atoms and a planar location 1.03 Å from the nitrogen atom. Full-matrix, least-squares refinement based on anisotropic temperature factors for the iodine atom and fixed hydrogen parameters led to final weighted and unweighted R factors of 6.3% and 5.1%. The positional parameters with their standard deviations from this analysis are listed in Table I and the bond distances and angles with their standard deviations in Figure 1. The five-mem-

Table I. Final Atomic Parameters for Iodomethylpyrrolid-2-one

	x	y	z	B,[a] Å²
I	0.1396 (1)	0.0704 (1)	1.0813 (2)	
O	0.304 (1)	0.461 (1)	0.687 (2)	4.7 (2)
N_1	0.130 (1)	0.385 (1)	0.858 (1)	3.6 (2)
C_2	0.206 (1)	0.389 (1)	0.700 (2)	3.3 (2)
C_3	0.156 (1)	0.298 (1)	5.549 (2)	4.3 (2)
C_4	0.046 (1)	0.220 (2)	0.643 (2)	5.0 (3)
C_5	0.018 (1)	0.298 (1)	0.836 (2)	4.0 (2)
C_6	−0.099 (1)	0.215 (2)	1.007 (2)	4.3 (3)
H_1	0.151	0.438	0.983	4.5
H_2	0.228	0.228	0.498	4.5
H_3	0.121	0.360	0.428	4.5
H_4	−0.039	0.220	0.550	4.5
H_5	0.072	0.113	0.671	4.5
H_6	−0.064	0.366	0.811	4.5
H_7	−0.097	0.158	0.983	4.5
H_8	−0.024	0.286	1.128	4.5

[a] The anisotropic thermal motion is expressed in the form exp $[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$ Å², where β_{11} = 0.0112 (1), β_{22} = 0.0107 (1), β_{33} = 0.0337 (3), β_{12} = 0.0014 (1), β_{13} = 0.0048 (1), and β_{23} = 0.0003 (2).

---

[1] B. J. Litman and J. A. Schellman, *J. Phys. Chem.*, **69**, 978 (1965).

[2] D. W. Urry, *Annu. Rev. Phys. Chem.*, **19**, 477 (1968).

[3] D. W. Urry, *Proc. Nat. Acad. Sci. U. S.*, **60**, 394 (1968).

[4] D. W. Urry, *ibid.*, **60**, 1114 (1968).

[5] N. J. Greenfield and G. D. Fasman, *Biopolymers*, **1**, 595 (1969).

[6] D. Stigter and J. A. Schellman, *J. Chem. Phys.*, **51**, 3397 (1969).

[7] N. J. Greenfield and G. D. Fasman, *J. Amer. Chem. Soc.*, **92**, 177 (1970).

[8] D. F. Mayers and D. W. Urry, manuscript in preparation.

[9] A. F. Beecham, *Tetrahedron Lett.*, **55**, 4897 (1969).

[10] D. W. Urry, "Spectroscopic Approaches to Biomolecular Conformation," D. W. Urry, Ed., AMA Press, Chicago, Ill., 1970, p 92.

[11] W. C. Hamilton, *Acta Crystallogr.*, **18**, 502 (1965).

Table II. Final Atomic Parameters for L-Pyrrolid-2-one-5-carboxamide

	x	y	z	$\beta_{11} \times 10^3$	$\beta_{22} \times 10^3$	$\beta_{33} \times 10^3$	$\beta_{12} \times 10^3$	$\beta_{13} \times 10^3$	$\beta_{23} \times 10^3$
C_2	0.4210 (2)	0.6011 (9)	0.163 (1)	1.9 (1)	16 (1)	38 (3)	−0.5 (3)	1.1 (5)	−1 (2)
C_3	0.3842 (3)	0.7259 (9)	0.351 (1)	2.7 (2)	14 (1)	38 (3)	0.2 (4)	2.3 (6)	−5 (2)
C_4	0.3397 (3)	0.5821 (8)	0.502 (1)	2.6 (2)	13 (1)	42 (3)	0.1 (3)	2.9 (6)	−6 (2)
C_5	0.3727 (2)	0.3811 (8)	0.455 (1)	1.6 (1)	12 (1)	29 (2)	−0.4 (3)	0.1 (4)	−3 (1)
C_6	0.3217 (2)	0.2158 (8)	0.426 (1)	1.6 (1)	13 (1)	25 (2)	−0.1 (3)	0.4 (4)	1 (1)
N_1	0.4094 (2)	0.4081 (6)	0.217 (1)	1.8 (1)	7.2 (8)	39 (2)	0.2 (2)	2.5 (4)	3 (1)
N_2	0.3017 (2)	0.1387 (8)	0.650 (1)	2.5 (1)	21 (1)	27 (2)	−3.0 (4)	0.3 (4)	3 (1)
O_1	0.4549 (2)	0.6619 (6)	−0.017 (1)	3.3 (1)	12.9 (9)	51 (3)	−1.3 (3)	5.6 (5)	2 (1)
O_2	0.3004 (2)	0.1653 (6)	0.216 (1)	2.3 (1)	16 (1)	25 (2)	−2.3 (2)	−0.2 (3)	−1 (1)
H_2O	0.4580 (2)	0.0769 (6)	0.912 (1)	3.2 (1)	12 (1)	46 (2)	0.8 (3)	3.4 (5)	4 (1)
H_1	0.425	0.293	0.102	[a]					
H_2	0.355	0.837	0.253						
H_3	0.418	0.801	0.481						
H_4	0.339	0.618	0.704						
H_5	0.291	0.582	0.426						
H_6	0.406	0.347	0.613						
H_7	0.317	0.167	0.828						
H_8	0.267	0.033	0.633						

[a] The temperature factor assigned the hydrogen atoms was 3.0.

bered ring deviates from planarity to the extent that C_4 and C_5 are 0.18 Å and −0.06 Å out of the plane defined by the CON peptide atoms. The molecule packs in ribbons around the screw axes in the c direction. In each chain the oxygen of a given molecule is hydrogen bonded to the nitrogen of the molecule related by the screw axis.

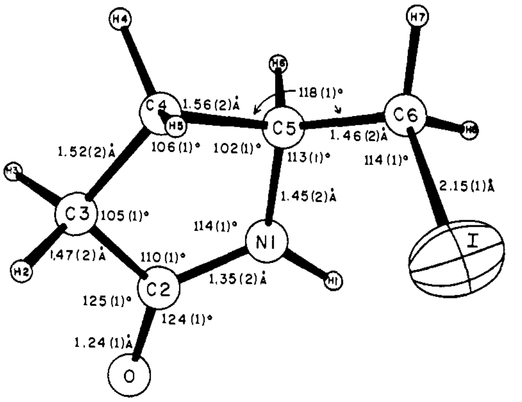


Figure 1. L-5-Iodomethylpyrrolid-2-one molecule with bond lengths and angles and their standard deviations. As drawn, the C_4 atom is 0.18 Å above the plane defined by the CON group.

L-Pyrrolid-2-one-5-carboxamide also crystallizes in the space group $P2_12_12_1$ with four molecules in the unit cell. The lattice constants, a = 20.43 (2), b = 6.743 (6), and c = 5.182 (5) Å, with four water and four carboxamide molecules in the unit cell, give a calculated density of 1.36 g/cm^3, which compares favorably with the observed density of 1.37 (1) g/cm^3, measured by flotation in $ZnCl_2$ solution. A crystal of dimensions 0.3 × 0.4 × 0.4 mm with a mosaic spread of up to 0.3° was used for data collection. A GE quarter-circle diffractometer with Ni-filtered Cu Kα radiation was used to scan manually the 720 peaks above background within the region of $2\theta < 140°$. The symbolic addition procedure[12] led to an E map which contained all but three of the nonhydrogen atoms. After full-matrix, least-squares refinement of the atoms, hydrogen atom positions were assigned as for the iodomethyl derivative, with the amide hydrogen atoms placed in the plane of the amide group. A difference map had shown peaks in the region of all but the two hydrogen atoms of the water molecule and H_1. In the final least-squares cycle the hydrogen parameters were fixed, but all other atoms were varied anisotropically to give weighted and a unweighted R factors of 10.0 and 6.6%. The designation of the oxygen and nitrogen atoms in the amide group is supported by the bond distances, the temperature factors, and the hydrogen atom peaks in the difference map. The final positional parameters with their standard deviations are listed in Table II and the bond distances and angles in Figure 2.

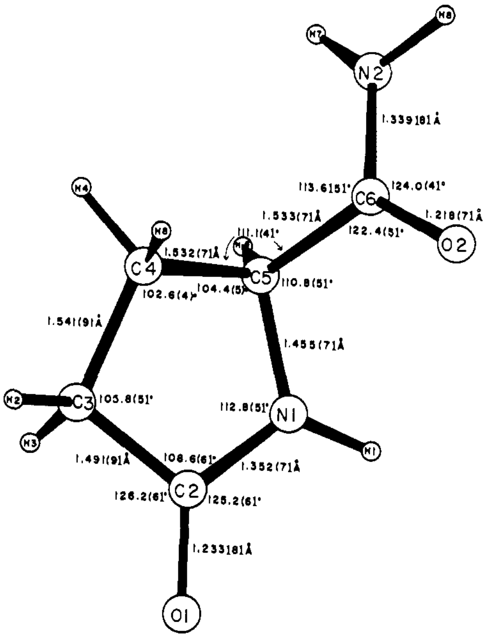


Figure 2. L-Pyrrolid-2-one-5-carboxamide molecule with bond lengths and angles and their standard deviations. As drawn, the C_4 atom is 0.23 Å above the plane defined by the peptide group.

The configuration of the five-membered ring is very similar to that of the iodo compound, with C_4 and C_5 0.23 and −0.17 Å out of the plane defined by the CON

---

(12) J. Karle and I. L. Karle, *Acta Crystallogr.*, **21**, 849 (1966).

peptide atoms. Statistically, the difference in the C_3–C_4–C_5 bond angles of the two pyrrolid-2-ones is not significant at the 99% probability level (2.58σ).[13] Hydrogen bonding occurs in ribbons among the carboxamide groups of molecules related by the screw axis in the *c* direction. Each water molecule interacts with three amide molecules—two with O_1 and one through H_1. The observed and final calculated structure factors for both of these compounds have been deposited with ASIS.[14]

Acknowledgments. We express appreciation to F. Grabiner for the collection of the data for L-pyrrolid-2-one-5-carboxamide, to D. Mayers for preparing the carboxamide crystals, and to NIH and ARPA for partial support.

---

(13) G. H. Stout and L. H. Jensen, "X-ray Structure Determination," MacMillan, Toronto, 1968, p 420.

(14) These tables have been deposited as Document No. NAPS-01065 with the ASIS National Auxiliary Publication Service, c/o CCM Information Corp., 909 3rd Ave., New York, N. Y. 10022. A copy may be secured by citing the document number and by remitting $2.00 for microfiche or $5.00 for photocopies. Advance payment is required. Make checks or money orders payable to CCMIC–NAPS.

J. A. Molin-Case, E. Fleischer, D. W. Urry
Department of Chemistry, University of Chicago
Chicago, Illinois 60637
Institute for Biomedical Research
Education and Research Foundation
American Medical Association, Chicago, Illinois 60610

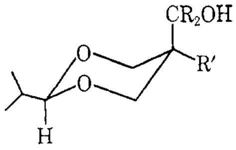
Received March 23, 1970

Effect of Dipolar and Bond Eclipsing Forces on Intramolecular Hydrogen Bonds

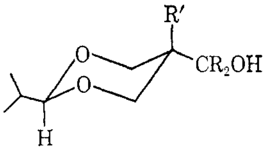
Sir:

Intramolecular hydrogen bonding is a well-known and well-reviewed[1] topic in chemistry. However, little is known regarding its interplay with other intramolecular interactions, such as bond eclipsing and dipole forces. We present here specific instances where bond eclipsing, acting in opposition to an intramolecular hydrogen bond, is shown to reduce the population of the hydrogen-bonding conformation; and where the combination of eclipsing and dipolar forces depopulates the hydrogen-bonded conformation further to the point where, in some instances, the bond cannot be perceived at all.

cis-5-Hydroxymethyl-2-isopropyl-1,3-dioxane (**1a**) has been shown,[2] by infrared spectroscopy, to be devoid of intramolecular hydrogen bonding[3] even though its lower homolog, 5-hydroxy-2-isopropyl-1,3-dioxane, shows only intramolecularly bonded and *no* free OH.[2,4]



1a, R = R′ = H
b, R = H; R′ = CH_3
c, R = CH_3; R′ = H



2a, R = R′ = H
b, R = H; R′ = CH_3
c, R = CH_3; R′ = H

We have now synthesized[5] compounds **1b**, **1c**, **2b**, and **2c**; their salient OH stretching frequencies in the infrared are shown in Table I.[6]

Table I. Hydroxyl Group Stretching Frequencies[a]

Compd	$\tilde{\nu}_{\text{free}}$, cm^{-1}	$\tilde{\nu}_{\text{bonded}}$, cm^{-1}
1a	3640	*b*
2a	3640	*b*
1b	3641	*b*
2b	3642	*b*
1c	3622	3571 (weak)
	3639[c]	
2c	3616	*b*
5	3623	*b*
6	3640	3530
7	3641	*b*

[a] Recorded on a Perkin-Elmer 521 double-beam grating spectrophotometer using matched 10-cm quartz cells. The concentration of substrate was 5.0 × 10^{-4} *M* in spectral grade CCl_4. The spectra were calibrated using the absorption peaks of *cis*-cyclohexane-1,2-diol at 3626 and 3588 cm^{-1}. [b] Absent. [c] Shoulder.

Compound **1b**, like **1a**, shows no intramolecular hydrogen bond at all.[3] The tertiary carbinol **1c** does display an intramolecularly bonded OH band, albeit a very weak one, along with much free OH, the latter apparently distributed over two different rotational conformations.

In **1c**, either the carbinol methyl groups or the oxygen atom may point into the ring; only in the latter situation is intramolecular hydrogen bonding possible. Three lines of evidence suggest that it is, in fact, the oxygen which points inward. First, it has been calculated[7] that the methyl-inside conformation is destabilized by 2.3 kcal/mol. Secondly, and in contrast to all the other cases, the major stretching frequency for unbonded OH in **1c** (3622 cm^{-1}) is in poor agreement with that calculated[6] (3605–3617 cm^{-1}). Thirdly, and most significantly, the chemical shift (proton nmr, 60 MHz, measured in CCl_4 solution relative to TMS) of the carbinol methyl group in **1c** changes dramatically, from 82.7 to 68.7 Hz, upon dilution from *ca.* 1 *M* to 5.5 × 10^{-3} *M*. We ascribe this to a change from the predominantly "OH-outside" con-

---

(1) (a) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, New York, N. Y., 1960, Chapter 5; (b) M. Tichy, *Advan. Org. Chem.*, **5**, 115 (1965).

(2) E. L. Eliel and M. K. Kaloustian, *Chem. Commun.*, 290 (1970); E. L. Eliel, paper presented at the International Symposium on Conformational Analysis, Brussels, Belgium, Sept 11, 1969.

(3) Similar results have been observed by (a) P. Laszlo, personal communication, Oct 7, 1969; R. Dratler and P. Laszlo, *Tetrahedron Lett.*, in press; (b) J. Delmau, personal communication, Nov 5, 1969. Both Laszlo and Delmau worked with an unbiased system (5-methyl-5-hydroxymethyl-1,3-dioxane, analogous to **1b**/**2b** without the 2-isopropyl group). Laszlo has adduced spectral evidence that this compound does, in fact, exist predominantly in the CH_2OH axial conformation (analogous to **1b**). Unpublished work from our laboratory (R. Enanoza) confirms that in the **1b** $\rightleftharpoons$ **2b** chemical equilibrium, **1b** predominates by 0.68 kcal/mol.

(4) S. A. Barker, J. S. Brimacombe, A. B. Foster, D. H. Whiffen, and G. Zweifel, *Tetrahedron*, **7**, 10 (1959).

(5) Preparation of **1b** and **2b** by Mr. R. Enanoza involved condensation of 2-methylene-1,3-propanediol (kindly donated by Professor J. P. Fleury, Mulhouse, Switzerland) with isobutyraldehyde followed by oxymercuration–demercuration according to H. C. Brown, *et al.*, *J. Amer. Chem. Soc.*, **89**, 1522, 1524, 1525 (1967). The stereoisomers were separated by preparative glpc. Treatment of pure *cis*- and *trans*-5-carbomethoxy-2-isopropyl-1,3-dioxane[2] with 2 equiv of MeMgI gave **1c** and **2c**, respectively, in good yields. Elemental and spectral analyses for all new compounds were in agreement with the postulated structures.

(6) Except in the case of **1c**, the stretching frequencies for the unbonded OH in the compounds in Table I were within the range calculated according to L. Joris, P. v. R. Schleyer, and E. Osawa, *Tetrahedron*, **24**, 4759 (1968), for the largest number of possible rotational isomers. In the case of **1c**, shown to be mainly in conformation **3**, prediction according to Schleyer's rules is not possible.

(7) See E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, **90**, 3444 (1968), footnote 43.