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Neutron Diffraction at 23 K and *ab initio* Molecular-Orbital Studies of the Molecular Structure of Acetamide

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Abstract

The crystal structure of the rhombohedral form of acetamide has been refined using single-crystal neutron diffraction data at 23 K. The internal thermal motion of the hydrogen atoms was larger than anticipated, with a 15° r.m.s. oscillation of the methyl group and a 7° r.m.s. oscillation of the amide group, determined by a segmented-body thermal-motion analysis. The orientation of the methyl group is such that one C—H bond is normal to the plane of the non-hydrogen atoms. The observed and thermally corrected bond lengths (in Å) are C—C, 1·509 (1), 1·513; C—N, 1·335 (1), 1·337; C=O, 1·247 (1), 1·250; C—H, 1·085 (2), 1·125; 1·076 (2), 1·119; N—H, 1·023 (2), 1·036. *Ab initio* molecular-orbital calculations were carried out at the Hartree–Fock 3-21G level. The lowest energy conformation for the isolated molecule is different from that observed in the crystal, being that with *m* symmetry having one C—H bond eclipsed to the carbonyl bond. The conformation in the crystal structure was calculated to be 1·7 kJ mol^{-1} higher in energy. The theoretically optimized bond lengths (in Å) for the observed conformer were C—C, 1·516; C—N, 1·358; C=O, 1·216; C—H, 1·085, 1·080; N—H, 0·997, 0·994. The significant differences between experimental and theoretical C=O and C—N bond lengths of 30σ and 20σ may be due, in part, to the hydrogen bonding in the crystal. There is also a significant discrepancy between the thermally corrected C—H and N—H bond lengths and the theoretical values.

Introduction

The crystal structure of the rhombohedral form of acetamide was determined by Senti & Harker (1940) and was refined by Denne & Small (1971) using room-temperature X-ray data. Ottersen (1975) carried out a low-temperature X-ray refinement at 108 K. A gas-phase electron diffraction structure analysis of acetamide has been reported by Kitano & Kuchitsu (1973).

Several *ab initio* molecular-orbital studies of the structure of acetamide have been reported. Radom, Lathan, Hehre & Pople (1972) and also Hagler, Leiserowitz & Tuval (1976) have examined the torsional rotational potential of the methyl group. Ottersen (1975) carried out a partial geometry optimization at the Hartree–Fock level with a double-zeta type basis set. He noted significant differences between the theoretical and experimental (X-ray) C=O and C—N bond lengths. However, bond angles and the C—H and N—H lengths were assigned assumed values in the calculations.

In the present work, we make a fuller comparison between theoretical and crystallographic data on acetamide. A new crystal structure refinement at 23 K is described, together with a complete *ab initio* molecular-orbital geometry optimization. These results are also compared with other theoretical and experimental data on the related smaller molecules, formamide, acetaldehyde, and formaldehyde.

Experimental

Data collection and refinement

Crystallization by slow cooling (318 to 295 K) of a saturated ethyl acetate–ethanol solution of acetamide gave hexagonal prisms, elongated along the [001] direction, with eight faces ({100} and {001}). A specimen (4·55 × 1·25 × 0·95 mm) was cut from a longer fragment for neutron data collection. The data

Table 1. *Crystal data for rhombohedral acetamide*

Space group $R3c$, $Z = 18$ (hexagonal cell)

Hexagonal cell dimensions (in Å) and expansion coefficients

	This work	Ottersen (1975)	Denne & Small (1971)	
	23 K	108 K	173 K	298 K
a	11·513 (3)	11·516 (2)	11·536 (5)	11·526 (5)
c	12·883 (4)	13·091 (2)	13·194 (5)	13·589 (5)
$\alpha_a =$	4·06 10^{-6} K^{-1}			
$\alpha_c =$	0·198 10^{-3} K^{-1}			

were measured at the Brookhaven High Flux Beam Reactor with a monochromated beam obtained by reflection from the (002) planes of beryllium. The neutron wavelength of 1·0445 (1) Å was determined by least-squares fit of diffraction setting-angle data for 30 reflections of a standard KBr crystal ($a_0 = 6·6000$ Å). The acetamide crystal was mounted within a few degrees of the hexagonal c axis on an Al pin and enclosed under helium in an Al can. This assembly was attached to the cold finger of a closed-cycle refrigerator* which was then positioned inside the χ-circle of the diffractometer. The crystal was cooled over a period of 4 h and maintained at 22·6 ± 0·5 K for one week. Calibration of the platinum resistance thermometer was based on the observed magnetic transition of FeF_2 (78·4 K; Hutchings, Shulhof & Guggenheim, 1972).

The lattice parameters given in Table 1 were determined by least-squares fit to the neutron diffractometer $\sin^2\theta$ values for 31 reflections with $46° < 2\theta < 49°$. The neutron integrated intensities were measured for the primitive rhombohedral cell using a $\theta/2\theta$ step-scan method in which counts at each step were accumulated for a preset monitor count of the direct beam. Scan widths of $\Delta(2\theta) = 3·0°$ were used for reflections with $\sin\theta/\lambda \le 0·40$ Å^{-1} and were varied according to the dispersion formula $\Delta(2\theta) = (1·597 + 3·101 \tan\theta)°$ for reflections with $0·40$ Å$^{-1} < \sin\theta/\lambda \le 0·86$ Å^{-1}. The variance in an intensity was derived from counting statistics. Neutron absorption corrections were applied using an analytical procedure (de Meulenaer & Tompa, 1965; Templeton & Templeton, 1973). The linear absorption coefficient ($\mu = 176$ m^{-1}) was calculated assuming the mass absorption coefficient for chemically bonded hydrogen to be 2·39 m^2 kg^{-1} (McMullan, Fox & Craven, 1978). The resulting crystal transmission factors ranged from 0·73 to 0·81. Intensities were measured for 640 independent reflections with all positive hexagonal indices.

Full-matrix least-squares refinement in space group $R3c$ was carried out with a modified version of the computer program of Busing, Martin & Levy (1962). The quantity minimized was $\sum w\Delta^2$, where $\Delta = (F_{\rm obs})^2 - (F_{\rm calc})^2$ and $w = 1/\sigma^2(F^2)$, with $\sigma(F^2) = [\sigma^2_{\rm counter} + (0·01F^2_{\rm obs})^2]^{1/2}$. The neutron scattering lengths (in fm) used were 6·65 for carbon, 9·40 for nitrogen, 5·803 for oxygen, and −3·74 for hydrogen (Shull, 1972). The initial values for the positional parameters were those reported by Denne & Small (1971); isotropic temperature factors (U) of 0·0095 Å^2 for non-hydrogen atoms and 0·0127 Å^2 for hydrogen atoms were assumed. The parameters varied in the final refinement included one scale factor, 26 positional parameters (z of nitrogen being fixed to define the origin in the polar direction), 54 anisotropic temperature factors, and the 6 anisotropic extinction parameters for a type I crystal with Lorentzian distribution of mosaicity (Becker & Coppens, 1975). There were no changes greater than $0·2\sigma$ in any of the 87 parameters varied in the final refinement cycle. The agreement factors were $R(F) = 0·021$, $R(F^2) = 0·027$, $wR(F) = 0·017$, $wR(F^2) = 0·033$, and $[(\sum w\Delta^2)/(N_{\rm obs} - N_{\rm param})]^{1/2} = 1·454$. Extinction was significant, with 19 reflections having correction factors between 0·90 and 0·70. The most severe correction ($0·70F^2_{\rm calc}$) was for the reflection 006. The atomic parameters are given in Table 2.* The thermal-motion ellipsoids and atomic notation are shown in Fig. 1.

The thermal-motion analysis

With the four non-hydrogen atoms in a plane, the rigid-body analysis gives rise to a singularity. The segmented-body analysis method (Johnson, 1970) was therefore used initially to obtain experimental estimates of the non-torsional internal motions of the hydrogen

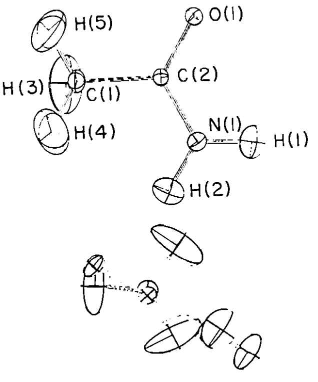

Fig. 1. Thermal ellipsoids for acetamide (hexagonal form) at 23 K, shown at 75% probability (Johnson, 1976). Top: atomic notation and view perpendicular to C, N, O plane. Bottom: view in direction of C(2)—C(1) bond.

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* Air Products & Chemicals Inc. DISPLEX® Model CS-202.

* Tables of observed and calculated structure factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35365 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Final atomic parameters for acetamide at* 23 K

The fractional coordinates are $\times 10^5$ for non-hydrogen atoms, $\times 10^4$ for hydrogen atoms. Anisotropic temperature factors ($Å^2 \times 10^4$ for non-hydrogen atoms, $\times 10^3$ for hydrogen atoms) are referred to the crystal axes and correspond to the temperature-factor expression $T = \exp(-2\pi^2 \sum_i^3 \sum_j^3 h_i h_j a_i^* a_j^* U_{ij})$. Estimated standard deviations given in parentheses refer to the least significant digit.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	47665 (8)	12990 (8)	3599 (9)	65 (3)	66 (3)	101 (3)	12 (2)	−1 (3)	1 (3)
C(2)	34109 (7)	387 (7)	3924 (9)	45 (3)	47 (3)	67 (2)	17 (2)	−1 (3)	1 (3)
O(1)	24111 (9)	−60 (11)	−229 (7)	57 (4)	62 (4)	112 (4)	26 (3)	−16 (3)	9 (3)
N(1)	33393 (7)	−10004 (6)	9090 (0)	70 (2)	71 (2)	106 (2)	31 (2)	−5 (2)	21 (2)
H(1)	2429 (2)	−1829 (2)	1062 (2)	15 (1)	15 (1)	28 (1)	3 (1)	1 (1)	5 (1)
H(2)	4182 (2)	−931 (2)	1235 (2)	15 (1)	21 (1)	27 (1)	10 (1)	−5 (1)	4 (1)
H(3)	4879 (3)	1885 (2)	1051 (2)	37 (1)	30 (1)	33 (1)	−1 (1)	5 (1)	−18 (1)
H(4)	5575 (2)	1084 (2)	351 (3)	17 (1)	26 (1)	90 (2)	11 (1)	4 (1)	3 (1)
H(5)	4838 (3)	1908 (3)	−298 (2)	35 (1)	30 (1)	35 (1)	−2 (1)	−9 (1)	20 (1)

atoms, which were then subtracted out before attempting to fit the torsional segmented-body model. In the initial analysis, the nine atoms were grouped into three segments (the non-hydrogen atoms, the amide hydrogens and the methyl hydrogens), with three flexible joints interconnecting the segments and the stationary lattice.

Assuming a C—H and N—H r.m.s. stretch correction of 0·076 Å (Cyvin, 1968), the NH_2 r.m.s. 'scissor' correction (in the molecular plane) was calculated to be 0·105 Å and the C—H r.m.s. inward-bending towards the CH_3 axis was 0·120 Å from the riding rotation of the segments. The above corrections for the internal motion of the hydrogen atoms were then subtracted from the r.m.s. displacements before fitting the segmented-body model described below.

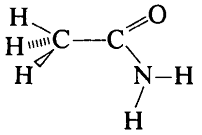
The segmented model used had three torsional degrees of freedom consisting of the CH_3, C=O, and NH_2, with three flexible joints, two between the segments and one from the central carbon atom to the stationary lattice. The overall fit was good, with $\langle \text{r.m.s. } U_{ij} - U_{ij_{\text{SBM}}} \rangle = 0{\cdot}0006$ Å^2 without a screw coupling between the motion of the methyl group and the parent segment, and 0·00047 Å^2 with $\sigma(U_{ij}) = 0{\cdot}00035$ Å^2 when this coupling was included. The r.m.s. torsion of the NH_2 group about the C—N bond was 7°, that of the CH_3 group about the C—C bond was 15°. With the internal torsion and hydrogen vibration motion subtracted, the rigid-body motion of the segment consisting of the C, O, and N atoms only was as shown below, based on orthonormal axes.

		a_1	a_2^*	c
T	0·082 Å	79·1°	96·8°	12·9°
	0·075	16·3	100·8	102·0
	0·067	78·0	12·8	85·5
ω	3·5°	78·0	145·5	58·2
	2·6	128·1	121·9	125·7
	2·0	40·6	101·8	128·2

The translation motion was very similar to that measured in erythritol, $(H_2C.OH.CHOH)_2$, by neutron diffraction at 20 K (Ceccarelli, Jeffrey & McMullan, 1980), but the libration amplitudes are greater by a factor of two.

Ab initio molecular-orbital calculations

The potential surface of acetamide was explored at the Hartree–Fock level using the 3-21G split-valence basis (Binkley, Pople & Hehre, 1980). This is the HF/3-21G theoretical model, as incorporated in the *GAUSSIAN* 78 program (Binkley, Whiteside, Krishnan, Seeger, DeFrees, Schlegel, Topiol & Pople, 1980). All geometrical parameters were adjusted to minimize the calculated total energy. This led to the structure (I) with a methyl C—H bond eclipsing C=O.


(I)

The geometrical parameters are listed in Table 3; the corresponding total energy is −206·81594 hartree (1 hartree ≡ 4·35916 × 10^{-18} J). The complete second-derivative matrix was evaluated for this structure (Pople, Krishnan, Schlegel & Binkley, 1979), and found to have no negative eigenvalues, thereby confirming that (I) is a minimum on the full potential surface.

A second HF/3-21G structure was determined with the methyl group held in the conformation found in the crystal, *i.e.* with the HCC plane perpendicular to the CCO plane. Energy minimization with respect to all other geometrical parameters led to a second structure also listed in Table 3. The total energy for this conformer is −206·81531 hartree.

Table 3. *Experimental (hexagonal crystal structural) and theoretical molecular dimensions of acetamide*

The σ values in parentheses refer to the least significant figures.

	Experimental at 23 K		Theoretical (HF/3-21G)		ED data*
	Observed	Corrected	Minimum energy CH_3 conformation	Observed CH_3 conformation	
Bond lengths (Å)					
C(1)–C(2)	1·5094 (10)	1·513	1·515	1·516	1·519 (6)
C(2)–O(1)	1·2468 (12)	1·250	1·215	1·216	1·220 (3)
C(2)–N(1)	1·3351 (11)	1·337	1·360	1·358	1·380 (4)
C(1)–H(3)	1·085 (2)	1·125	1·079†	1·085	1·124 (10)
C(1)–H(4)	1·076 (2)	1·119	1·084	1·082	
C(1)–H(5)	1·076 (2)	1·119	1·084	1·079	
N(1)–H(1)	1·023 (2)	1·036	0·997	0·998	1·022 (11)
N(1)–H(2)	1·023 (2)	1·037	0·994	0·994	
Bond angles (°)					
C(1)–C(2)–O(1)	121·1 (1)	§	123·5	122·9	123·0 or 125·9
C(1)–C(2)–N(1)	116·5 (1)		113·8	114·4	115·1 (1·6) or 112·2 (1·6)
O(1)–C(2)–N(1)	122·3 (1)		122·7	122·7	122·0 (6)
C(2)–C(1)–H(3)	108·6 (2)		108·7	109·0	109·8 (2·0)
C(2)–C(1)–H(4)	112·1 (1)		110·3	112·2	
C(2)–C(1)–H(5)	110·7 (2)		110·3	108·7	
H(3)–C(1)–H(4)	107·7 (3)		109·5	108·9	
H(3)–C(1)–H(5)	107·2 (2)		109·5	108·1	
H(4)–C(1)–H(5)	110·4 (3)		108·5	109·9	
C(2)–N(1)–H(1)	120·5 (1)		118·8	118·6	118·5‡
C(2)–N(1)–H(2)	120·2 (1)		122·5	122·8	120·0‡
H(1)–N(2)–H(2)	118·9 (1)		118·7	118·6	
Torsion angles (°)					
H(3)–C(1)–C(2)–O(1)	92·4		0·0	90·0‡	0·0‡
H(3)–C(1)–C(2)–N(1)	−85·9		180·0	−87·9	180·0‡
H(1)–N(1)–C(2)–O(1)	−8·2		0·0	−0·3	0·0‡
H(2)–N(1)–C(2)–O(1)	179·5		180·0	180·2	180·0‡

* Kitano & Kuchitsu (1973).

† H(3) denotes the in-plane hydrogen.

‡ Assumed values.

§ The thermal-motion corrections for the valence and torsion angles were insignificant.

Before we proceed to compare these theoretical results with those from the crystallographic studies, it is desirable to check that the HF/3-21G model is adequate to describe structural parameters in the smallest molecules containing the same bonds, where experimental data are very good. Table 4 gives such a comparison for bond lengths, including values obtained with more sophisticated theoretical models. These are HF/6-31G* (using the larger 6-31G* basis with *d*-type polarization functions on non-hydrogen atoms) and MP2/6-31G* (allowing for the effects of electron correlation at the second-order Møller–Plesset perturbation level). The comparison shows excellent agreement between HF/3-21G lengths and the spectroscopic values. However, this high accuracy of the sample theory results from some cancellation of errors due to basis-set deficiency (HF/3-21G → HF/6-31G* leads to bond shortening) and neglect of electron correlation (HF/6-31G* → MP2/6-31G* leads to lengthening). Nevertheless, Table 4 suggests that HF/3-21G theory should give a good representation of the equilibrium structures of larger molecules such as acetamide *in isolation*.

Discussion of the crystal structure results

The bond lengths and valence angles involving the non-hydrogen atoms, given in Table 3, are in agreement with those determined by the X-ray analysis of Ottersen (1975), within the standard deviations of that experiment. The non-hydrogen framework is distorted slightly from planarity, with C(2) out of the plane of C(1), O(1) and N(1). The deviations (in Å) from the least-squares best plane through these atoms are: C(2), +0·009 (1); C(1), −0·002 (1); O(1), −0·003 (1); N(1),

Table 4. *Test of* HF/3-21G *theory on some small-molecule bond lengths* (Å)

Bond	Molecule	HF/3-21G Binkley, Pople & Hehre (1980)	HF/6-31G* DeFrees *et al.* (1979)	MP2/6-31G* DeFrees *et al.* (1979)	Spectroscopic Harmony *et al.* (1979)
C—H	Methane	1·083	1·084	1·090	1·094
N—H	Ammonia	1·002	1·002	1·017	1·012
C—C	Ethane	1·542	1·528	1·526	1·526
C—N	Methylamine	1·471	1·453	1·465	1·471
C=O	Formaldehyde	1·207	1·184	1·221	1·206

Table 5. *Hydrogen-bonding dimensions in acetamide at* 23 K

The estimated standard deviations are 0·002 Å and 0·2°.

	(N)H···O	∠N—H···O	∠H···O=C	∠H···O=C—C
H(1)	1·895 Å	167·1°	123·8°	−6·8°
H(2)	1·866	171·4	126·1	158·9

−0·003 (1). The amide group is slightly pyramidal, with deviations from the best plane of N(1), +0·032 (1); C(2), −0·009 (1); H(1), −0·012 (1); H(2), −0·012 (1). The torsion angles O(1)—C(2)—N(1)—H(1), −8·2, and O(1)—C(2)—N(1)—H(2), 179·5°, show that H(1) is significantly out of the N—C=O plane.

The methyl group is oriented with the C—H(3) bond nearly normal to the non-hydrogen molecular plane. The relevant torsion angles are H(3)—C(1)—C(2)—O(1), 92·4; H(3)—C(1)—C(2)—N(1), −85·9; H(5)—C(1)—C(2)—O(1), −25; H(4)—C(1)—C(2)—N(1), +33°, indicating a twist of 4° from the symmetrical orientation in a clockwise direction along C(2)—C(1). The C—H(3) bond, normal to the plane, is longer than the other two by about 4σ, and all valence angles involving H(3) are less than tetrahedral. Due to the large oscillatory motion, the thermal-motion corrections to the C—H bond lengths are unusually large. The uncorrected non-bonded distances O(1)···H(1), O(1)···H(5), N(1)···H(4), C(1)···H(2) are almost equal, 2·538, 2·575, 2·593 and 2·566 Å, respectively.

The hydrogen-bonding distances are given in Table 5. The two hydrogen bonds and the C=O bond are approximately planar and trigonal with respect to the carbonyl oxygen, with the plane twisted by about 15° to the molecular plane. The uncorrected N—H and H···O distances are normal and are close to the mean values when compared with the plot of the corresponding distances observed in the crystal structures of the α-amino acids (*cf.* Figs. 8.3 and 9.4, Olovsson & Jönsson, 1976; Koetzle & Lehmann, 1976).

As shown in Fig. 1 of Denne & Small (1971), the hydrogen bonds form hexagons in the *ab* plane. The differences in unit-cell dimensions given in Table 1 indicate a relatively small coefficient of expansion in the *ab* plane relative to that in the *c* axis direction.

Comparison of experimental and theoretical results

We first consider the conformation of the methyl group in acetamide. The theoretical energy minimum is that with *m* symmetry, having one of the methyl C—H bonds eclipsed to the C=O bond. The conformation observed in the crystal, with a C—H anticlinal to C=O, is calculated to be 1·7 kJ mol^{-1} higher. This is consistent with the low barriers previously found without full optimization, 1·3 kJ mol^{-1} by Radom, Lathan, Hehre & Pople (1972) with the 4-31G basis, and 0·4–0·8 kJ mol^{-1} by Hagler, Leiserowitz & Tuval (1976) with 6-31G. It is also consistent with qualitative arguments based on perturbation molecular-orbital theory (Hehre, Pople & Devaquet, 1976). The observed conformation is probably determined by crystal-packing forces, as found in a recent theoretical study by Caillet, Claverie & Pullman (1978). It would be interesting to know whether the same conformation occurs in the orthorhombic form of acetamide (Hamilton, 1965).

We next compare theoretical and experimental bond lengths in acetamide and the related smaller molecules, formamide, acetaldehyde, and formaldehyde. This comparison, including other experimental studies (electron diffraction, ED, and microwave spectroscopy, MW), is presented in Table 6. Although there is good agreement for C—C bond lengths, there are significant differences between the sets of results for the C=O and C—N lengths. Here the discrepancies between the theoretical and experimental bond lengths are 30σ and 20σ, respectively. In contrast to the C—C lengths, application of thermal-motion corrections increases the discrepancies, as shown in Table 3. The agreement between theoretical values and gas-phase experimental results (ED for all, and MW for smaller molecules) for the C=O and C—N bond lengths is better than with the crystal data. The solid-state results give longer C=O bonds and shorter C—N bonds than the theory or gas-phase results, which suggests that these differences may be a consequence of the

Table 6. *Bond-length comparisons* (Å) *for acetamide and related molecules*

For consistency with the electron diffraction (ED) and microwave (MW) data, the error estimates, given in parentheses, are 2·5σ (*i.e.* the 99% confidence level).

Bond	Molecule	Crystal	ED	MW	Theory (HF/3-21G)
C—C	Acetamide	1·513 (3)^{a} 1·510 (8)^{b}	1·519 (6)^{c}		1·516
	Acetaldehyde		1·514 (5)^{d}	1·501 (5)^{e}	1·507
C=O	Acetamide	1·250 (4)^{a} 1·243 (12)^{b}	1·220 (3)^{c}		1·216
	Formamide	1·241 (4)^{f} 1·243 (6)^{b}	1·212 (3)^{g}	1·219 (12)^{h}	1·212
	Acetaldehyde		1·209 (3)^{d}	1·216 (2)^{e}	1·209
	Formaldehyde		1·209 (3)^{i}	1·208 (3)^{j}	1·207
C—N	Acetamide	1·337 (3)^{a} 1·336 (12)^{b}	1·380 (4)^{c}		1·358
	Formamide	1·318 (3)^{f} 1·319 (5)^{b}	1·368 (3)^{g}	1·352 (12)^{h}	1·353
N—H	Acetamide	1·036 (5)^{a}	1·022 (11)^{c}		0·995
	Formamide		1·027 (6)^{g}	1·002 (3)^{h}	0·996
C—H	Acetamide	1·121 (5)^{a}	1·124 (10)^{c}		1·082
	Acetaldehyde			1·087 (5)^{e}	1·084

(*a*) This work; (*b*) Ottersen (1975); (*c*) Kitano & Kuchitsu (1973); (*d*) Iijima & Kimura (1969); (*e*) Kilb, Lin & Wilson (1975); (*f*) Stevens (1978); (*g*) Kitano & Kuchitsu (1974); (*h*) Hirota, Sugisaki, Nielsen & Sorensen (1974); (*i*) Kato, Konaka, Iijima & Kimura (1969); (*j*) Takagi & Oka (1963).

hydrogen-bond formation in the crystalline state. A similar conclusion was reached by Ottersen (1975) from his comparison of theory with low-temperature X-ray results on acetamide and formamide, and by Stevens (1978) who carried out a charge-density study of formamide using low-temperature X-ray data.

As with the formic, acetic and propionic acid monomers and dimers, the hydrogen-bond formation appears to cause a redistribution of electron density in the molecules, which is manifested by a lengthening of the C=O acceptor bonds and a shortening of the C—*X*H donor bonds (Almenninger, Bastiansen & Motzfeldt, 1969; Derissen, 1971*a*,*b*; Beagley, 1975). This interpretation is consistent with the changes in the stretching-force constants with hydrogen bonding for C=O and C—N bonds in amides reported by Miyazawa, Shimanouchi & Mizushima (1956).

Studies of hydrogen bonding in a number of barbituric acid derivatives by Craven, Cusatis, Gartland & Vizzini (1973) provided evidence of small systematic variations in C—N bond lengths of 0·02 Å with hydrogen bonding, but the significance of these observations, ~3σ, was marginal. In the carbohydrates, there are three examples of non-hydrogen-bonded C—OH groups; in two of these the C—O distances of 1·414 (3) and 1·410 (2) Å are shorter than the mean values of 1·425 Å [C(4)—OH in methyl α-D-glucopyranoside (Jeffrey, McMullan & Takagi, 1977) and C(4)—OH in sucrose (Brown & Levy, 1973)], and in one a value of 1·432 (3) Å is observed [C(2)—OH in turanose (Kanters, Gaykema & Roelofsen, 1978)].

The effect of hydrogen bonding on *X*—H bond lengths is generally accepted (*cf.* Pimentel & McClellan, 1960) and recent neutron diffraction data have indicated that bond-length changes up to 0·05 Å are caused by hydrogen-bond formation (Olovsson & Jönsson, 1976; Koetzle & Lehmann, 1976). However, this evidence has to be evaluated with caution because of the difficulty of correcting for the thermal motion of the hydrogen atoms with the usual rigid-body and riding-motion methods (Busing & Levy, 1964). No conclusive evidence of O—H *versus* H···O dependence was obtained from recent neutron diffraction studies of carbohydrate crystal structures (Jeffrey, 1978).

There are significant differences of about 15σ between the experimental (crystal) and theoretical C—H and N—H bond lengths, when the thermal-motion corrections are applied. In the absence of these corrections, which are considerable, the agreement is almost within the limits of experimental errors. In the case of the N—H bonds, hydrogen bonding has been suggested to result in a lengthening of the order of 0·05 Å (see Fig. 8.13 in Olovsson & Jönsson, 1976). On the other hand, there remains a similar discrepancy between the thermally corrected C—H bond lengths of 0·02 Å (~10σ), for which we have no explanation. It is possible that the internal motion about the C—CH_3 and

C—NH_2 was over-emphasized by the segmented-body analyses. On the other hand, a neutron diffraction analysis of erythritol at 20 K, for which both rigid-body and segmented-body thermal analyses gave excellent fits (r.m.s. ΔU_{ij} of 0·0004 and 0·0007 Å^2), also gave corrected C—H bond lengths of 1·113 (2) and 1·115 (2) Å (Ceccarelli, Jeffrey & McMullan, 1980). The room-temperature neutron diffraction analysis of α-D-glucose gave segmented thermal-analysis-corrected values for the C—H bonds between 1·112 (4) and 1·127 (3) Å (Brown & Levy, 1979). Similar values of 1·115 to 1·118 Å were obtained from the room-temperature neutron diffraction study of glycolic acid, where corrections were made for the internal vibration in the molecule (Ellison, Johnson & Levy, 1971). In all cases where a more sophisticated attempt has been made to correct C—H bond lengths for thermal motion, the resulting values are significantly longer than the values obtained from high-level theoretical geometry optimizations of simple molecules (*e.g.* 1·090 Å in CH_4 and 1·090, 1·097 Å in CH_3OH; DeFrees, Levi, Pollack, Hehre, Binkley & Pople, 1979).

The agreement between the experimental and theoretical valence-angle geometry is generally good, with the largest discrepancies at C(2). In the C—H anticlinal model, the molecule is not constrained to *m* symmetry and can distort out of the plane. The small distortion shown by the calculated H(1)—N(1)—C(2)—O(1) torsion angle is much smaller than that observed. This difference could be due to crystal-field forces.

In summary, this comparison has revealed significant differences between experimental and theoretical C—N, C=O, C—H and N—H bond lengths in acetamide, which require further exploration by both experimenal investigations on related molecules and by theoretical modelling with simple molecules and hydrogen-bonded assemblages of these molecules.

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The Structure of 4-Thiopseudouridine

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Abstract

$C_9H_{12}N_2O_5S$ is in space group $P2_1$, with a = 15·434 (2), b = 7·4381 (5), c = 14·818 (2) Å, β = 110·45 (1)°, Z = 6, D_c = 1·627, D_o = 1·60 (3) Mg m^{-3}, V = 1593·9 Å^3, M_r = 260·3, λ(Mo $K\alpha_1$) = 0·70926 Å, T = 297 ± 1 K, F(000) = 816. The crystal structure of 4-thiopseudouridine, a thio-substituted derivative of the minor transfer RNA nucleoside pseudouridine, has been determined. The structure was solved by direct methods, but the determination was hampered by a high degree of pseudosymmetry in the crystal. The correct structure was chosen by refinement to an R of 0·043 for the 3972 significant data. The molecules are packed head to head and tail to tail, with the riboses hydrogen bonded and the bases stacked and hydrogen bonded in ribbons. The three independent molecules display no unusual conformational parameters.

Introduction

Pseudouridine is unique among the nucleosides in RNA in having a C—C 'glycosidic' bond, which gives it structural properties different from those of uridine. The synthetic nucleoside 4-thiopseudouridine has been shown by Wigler, Bindslev & Breitman (1974) to inhibit the growth of *Escherichia coli* (strain B5RU) when the cells are grown on pseudouridine. Wigler *et al.* have proposed that a metabolite of 4-thiopseudouridine, presumably the nucleotide, is an inhibitor of the enzyme pseudouridylate synthetase, which catalyzes the key reaction in the only known salvage pathway for pseudouridine 5′-phosphate (Solomon & Breitman, 1971), the conversion of pseudouridine 5′-phosphate to uridine 5′-phosphate. This study was undertaken to determine the conformational features of the 4-thio-substituted pseudouridine for comparison with pseudouridine and with other thio-substituted

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