Studies on the Molecular Structures of Gaseous Acetamide and N-methylacetamide by Electron Diffraction

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Introduction

In many problems of the structure of protein, it is essential to determine the probable dimension of the polypeptide chain. Recently Corey and Donohue carried out X-ray diffraction experiments on DL-alanine, L-threonine, β-glycylglycine and N-acetylglycine, and suggested the probable dimension of the polypeptide chain to be as follows1): C=O 1.23 Å, C-N 1.32 Å, αC—C 1.53 Å, αC—N 1.47 Å, ∠NCO 122°, ∠αCCO 121°, ∠CNαC 120° and ∠CαCN 110°. In the present investigation the molecular structure of gaseous acetamide, units of the polypeptide chain, and of gaseous N-methylacetamide, the simplest

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1) R. B. Corey, J. Donohue, *J. Am. Chem. Soc.*, **72**, 2899 (1950).

molecule with a peptide linkage, were determined by electron diffraction and were compared with the result obtained from the X-ray diffraction experiments of some proteins.

Senti and Harker[2] determined the structure of acetamide using X-ray diffraction by crystal to be as follows: C=O 1.28 Å, C—N 1.38 Å, C-C 1.53 Å, ∠NCO 122° and ∠CCO 129°. No reports have ever been published regarding the structure of N-methylacetamide.

Experiment

The boiling points of acetamide and N-methylacetamide are 222°C and 206°C respectively. These compounds were vaporized by the use of a high temperature nozzle shown in Fig. I. The temperature of vapors could easily be raised up to 200°C by heating a nichrome wire coiled around a sample holder. The amount of the vapor could be regulated by a needle.

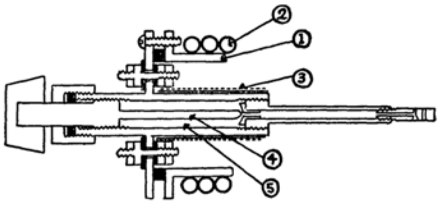

Fig. 1.—Diagram of the high temperature nozzle: (1) camera; (2) pipe coiled for coiled pipe for water cooling through which water is flowed; (3) nichrome wire; (4) needle; (5) sample holder.

The positions of maxima and minima of halos were estimated visually and were listed in Table 1. The visual curves are shown in Fig. 2V and Fig. 3v.

Table 1

Observed Values for Acetamide and N-methylacetamide*.

Max.	Min.	q		Max.	q	
		Acetamide	N-methylacetamide		Acetamide	N-methylacetamide
	2	15.36	14.14	6	53.23	53.30
2		19.40	18.65	7	61.54	60.15
	3	24.01	24.33	8	68.18	69.14
3		27.81	27.97	9	77.03	76.76
	4	31.96	31.45	10	84.67	86.15
4		36.35	35.31	11	93.00	94.13
	5	40.56	40.75	12	100.55	
5		44.37	44.26			
	6	49.16	49.27			

* The observed values for the 1st maximum and the 7th, 8th, 9th, 10th, 11th and 12th minima were inaccurate and were not listed in this table. These values were not used for quantitative comparison.

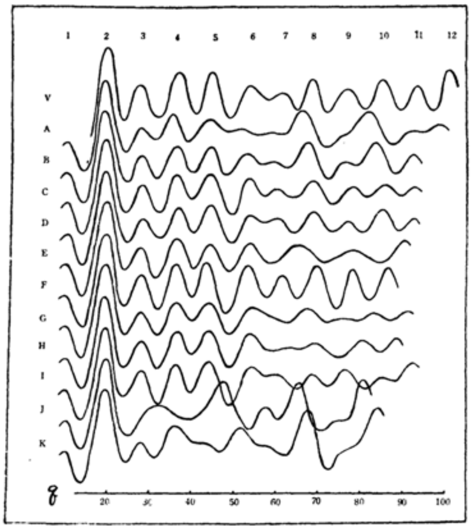

Fig. 2.—Visual and theoretical curves for acetamide.

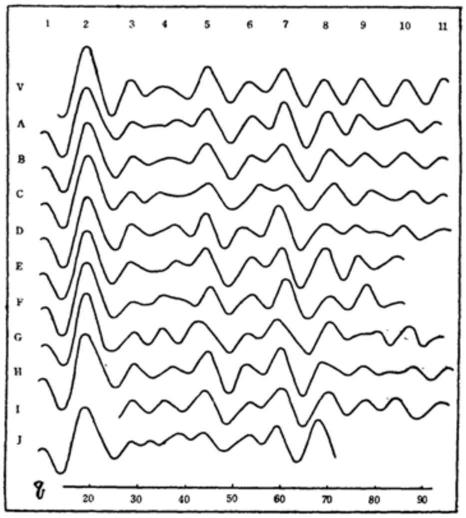

Fig. 3.—Visual and theoretical curves for N-methylacetamide.

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[2] F. Senti, D. Harker, *J. Am. Chem., Soc.*, **62**, 2008 (1940).

The theoretical intensity curves,

$$I(q)=\sum_{i}\sum_{\neq j}(Z_iZ_j/r_{ij})\exp(-a_{ij}q^2)\sin(\pi q r_{ij}/10)$$

were computed for various models and were compared with the visual curve. Here notations have their usual significances and $\exp(-a_{ij}q^2)$ is a factor relating to the intramolecular vibration.

Because the theoretical intensity curves for acetamide were not affected appreciably by vibrations, a_{ij}'s could be taken as zero. For N-methylacetamide, the rotational vibration about carbon nitrogen bond cannot be neglected, therefore a a_{ij}'s were taken as either zero or 0.0004 for both C—C pair and C—O pair (Fig. 4).

Table 2
Models Assumed for Acetamide

model	C—N (Å)	C=O (Å)	C—C (Å)	∠NCO (degree)	∠CCO (degree)
A	1.37	1.25	1.54	122	120
B	„	1.23	1.54	124	122
C	„	1.21	1.54	126	120
D	„	„	1.52	124	124
E	„	„	1.57	126	118
F	„	1.21	1.54	128	120
G	„	„	„	124	120
H	„	„	„	126	118
I	„	1.19	1.54	126	124
J	1.38	1.28	1.53	122	129
K	1.32	1.23	1.53	122	121

Table 3
Models Assumed for N-methylacetamide

model	C—N (Å)	∠CNC (degree)	
A	1.45	115	trans
B	„	„	trans, vibrating
C	„	110	trans, rigid
D	„	120	trans, rigid
E	1.49	115	trans, rigid
F	1.39	„	trans, rigid
G	1.45	115	cis, rigid
H	„	„	twisted by 30 degrees from trans
I	„	„	free rotating
J	1.47	120	trans

Acetamide.—It was assumed that C-H 1.09 A, N-H 1.02 Å, ∠CCH 109°28′, ∠CNH 107° and that C, C, N and O atoms are coplaner. Because of many parameters involved, first the C—N distance was kept at 1.37 Å and the theoretical intensity curves were computed for various values of C-C, ∠NCO and ∠CCO, where the C=O distance was presumed to be 1.25 Å, 1.23 Å, 1.21 Å or 1.19 Å. Some of them are reproduced in Fig. 2.

(a) *Case of* C=O 1.25 Å: The theoretical curve for the model having the values of C-C 1.54 Å, ∠NCO 122° and ∠CCO 120° (Fig. 2A) did not agree with the visual curve, because the 6th and 7th maxima were too low; the 9th maximum appeared as a shelf and the q values of maxima were smaller than those in the visual curve. Even if different values were used for C—C, ∠NCO and ∠CCO with the values of model A, the 7th maximum disappeared and the theoretical curve in agreement with the visual curve could not be obtained.

(b) *Case of* C=O 1.23 Å: For the model having C—C 1.54 A, ∠NCO 124° and ∠CCO 122° (Fig. 2B), the theoretical curve obtained was similar in shape to the visual curve, except that the positions of maxima and minima disagreed with the observed values. If we assumed 1.57 Å for C—C distance, which was longer than the value of model B, the 8th, 9th and 11th maxima became higher, while the 6th and 7th maxima became lower. If we assumed 1.52 Å for C—C distance, which was shorter than the value of model B, the 6th, 7th, 8th, 10th, 11th and especially the 9th maxima became too low. These two theoretical curves appeared to be worse than the curve for model B. If C—C distance, ∠NCO and ∠CCO were varied properly, in the only case of about 1.52 Å, the theoretical curve could be obtained with the features similar to the visual curve. But the positions of maxima and minima shifted to q values smaller than the observed one.

(c) *Case of* C=O 1.21 Å: For the model having C—C 1.54 Å, ∠NCO 126° and ∠CCO 120° (Fig. 2C)∼124°, the theoretical curves showed good agreement with the visual curve in features and the positions of maxima and minima. In order to determine the acceptable range of parameters, C—C, ∠NCO, and ∠CCO, their values were varied from the values of model C. When ∠NCO and ∠CCO were kept at the value of model C and C—C distance was assumed to be 1.52 Å, no good theoretical curve could be obtained. But in this case, if ∠NCO and ∠CCO were varied properly, an acceptable theoretical curve could be obtained, for example, as shown in the curve of ∠NCO 124° and ∠CCO 124° (Fig. 2D). When ∠NCO and ∠CCO were kept at the value of model C and C—C distance was assumed to be 1.57 A, no curve could be obtained in agreement with the visual curve, even though we took any value of ∠NCO and ∠CCO (for example Fig. 2E). When C—C and ∠CCO were kept at the value of model C and ∠NCO was larger or smaller by two degrees than the angle of model C, acceptable theoretical curves could not be obtained as shown in Fig. 2F or G respectively. Finally if C—C and ∠NCO were kept at the value of model C and ∠CCO was smaller by two degrees than the angle of model C, no acceptable theoretical curve (Fig. 2H) could be obtained. In this case if ∠CCO was 126°, the theoretical curve was entirely similar to that of model H and therefore could not be accepted.

(d) *Case of* C=O 1.19 Å: For the model having C—C 1.54 Å, ∠NCO 126° and ∠CCO 124°, the theoretical curve (Fig. 2I) could be obtained in agreement to some extent with the visual curve, but it cannot be accepted as a better model from the point of view of the relations of the 8th and 9th, or of the 10th and 11th maxima.

Even though C—C, ∠NCO and ∠CCO were varied properly, satisfactory theoretical curves could not be obtained.

According to the results of interpretation outlined above, if we assume 1.37 Å for C—N distance, the value of 1.21 Å is the best and the values of 1.23 Å—1.19 Å are acceptable for C=O distance. For other parameters, ∠NCO, ∠CCO and C—C distance, fairly wide ranges of values are permissible to obtain theoretical curves similar to the visual one. Thus ∠NCO 128°~132°, C—C 1.50 Å~1.56 Å and ∠CCO 118°~126° may be adopted as the widest range of the values. Furthermore quantitative comparison with the visual curve was made for the positions of maxima and minima in several better theoretical curves.

Thus the structure of acetamide was determined as follows:

C=O	1.21 Å±0.02 Å,	∠NCO	125°±3°
C—N	1.36 Å±0.02 Å,	∠CCO	122°±4°
C—C	1.53 Å±0.03 Å,		
C—H	1.09 Å (assumed),	∠CCH	109°28′ (assumed)
N—H	1.02 Å (assumed),	∠CNH	107° assumed)

and C, C, N and O atoms assumed lying in one plane.

The structure obtained by Senti and Harker and the probable dimension of a polypeptide chain given by Corey and Donohue give theoretical curves shown in Fig. 2J and K respectively. They disagree definitely with the visual curve.

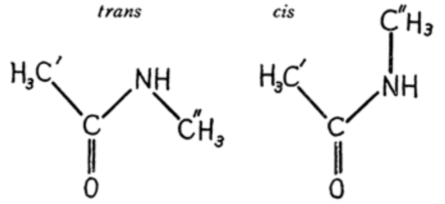

Fig. 4.—N-methylacetamide

N-methylacetamide. The photograph was analysed assuming a molecular structure similar to acetamide obtained above and using second C″—N distance, ∠C″NC and a rotational angle of the methylgroup about C″—N bond axis as parameters.

In the case of the trans configuration (Fig. 4), the theoretical curve having the values of C″—N 1.45 Å and ∠CNC 115° agreed to some extent with the visual curve, but the 4th and 11th maxima did not agree with those of the visual curve (Fig. 3A). If we took into account the rotational vibration of methyl group about C″—N bond axis, the theoretical curve was in satisfactory agreement with the visual curve (Fig. 3B). When C″—N was kept at 1.45 Å and ∠CNC was varied to 110° (Fig. 3C), even if we took the vibrational effect into account, no acceptable theoretical curve could be obtained. when C″—N was kept at 1.45 Å and ∠CNC was varied to 120° (Fig. 3D), the 7th maximum seemed to be too high compared with the 6th. But this model should not be discarded, entirely because, if the vibration is taken into account, the theoretical curve becomes more similar to the visual one than the theoretical curve for model 3D.

When ∠CNC was kept at the value of model A and C″—N distance was varied to 1.49 Å or 1.39 Å, the theoretical curves were obtained as shown in Fig. 3E and F respectively. Both curves are unacceptable.

In the case of the cis configuration (Fig. 4), the theoretical curve Fig. 3G was obtained using the same value of C″—N distance and ∠C″NC as model A. The curve was not in agreement with the visual one in regard to the positions of the 5th, 6th, 7th and 10th maxima and the feature of the 4th maximum. It could not be revised even if we took into account the rotational vibration of a methyl group. In the theoretical curve (Fig. 3H) computed for the model with the methyl group twisted by 30 degrees from the *trans* configuration, the 6th and 8th maxima shifted to smaller values and the similarity to the visual curve became worse in the feature of the curve. But the theoretical curves for the models with the methyl group twisted within about 30 degrees, could not be discriminated from the visual one. Further the theoretical curve for the model whose methyl group rotates freely about C—N bond axis (Fig. 3I), does not better account for the visual one than the curves for the *trans* configuration, but this also cannot be discarded.

According to the result mentioned above, it is most probable that N-methylacetamide has the trans configuration and its methyl group oscillates about C—N bond axis. But the structures whose methyl group rotates freely may also be probable. The conclusion from the measurement of dipole moment in solution[3] is that N-methylacetamide has the *trans* configuration. Further from the viewpoint of steric repulsion, the *trans* configuration is more favorable than the *cis* configuration.

with the known structure of acetamide the structure of N-methylacetamide was determined as follows:

C″—N	1.44 Å±0.04 Å
∠C″NC	117°±5°

trans configuration.

The theoretical curve for N-methylacetamide was computed using the structure of a polypeptide chain obtained by Corey and Donohue and is shown in Fig. 3J. It could be distinguished definitely from the visual curve.

Discussion of Results

Our results differ definitely from the values

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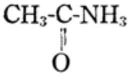
[3] S. Mizushima, T. Shimanouchi, S. Nagakura, K. Kuratani, M. Tsuboi, H. Baba, O. Fujioka, *J. Chem. Soc. Japan* **71**, 32 (1950); *J. Am. Chem. Soc.*, **72**, 3490 (1950).

obtained by Senti and Harker, but do not differ very much from the probable dimension of a polypeptide chain proposed by Corey and Donohue. The result obtained by Senti and Harker seems to be not very accurate. It has already been mentioned that the probable dimension of a polypeptide chain obtained by Corey and Donohue does not give a satisfactory theoretical curve.

The discrepancy between the results obtained by us and by Corey and Donohue may be supposed to be due to the difference in materials used and in the states of aggregation. Namely, Corey and Donohue used as samples β-glycylglycine, N-acetylglycine and so on while we used acetamide and N-methylacetamide morover they determined the crystal structures, while we determined the structures in the gaseous state.

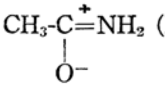
As it is unlikely that the former difference will give rise to an appreciable change in the molecular structure, it will be more adequate to consider that the latter is the main cause of the difference between the results obtained by us and by Corey and Donohue, i. e. to suppose that the hydgrogen bond, which is absent in the gaseous state but exists in the crystalline state, plays a major role

Acetamide will have the resonance structures shown by



$$\mathrm{CH_3\text{-}\underset{\substack{\| \\ O}}{C}\text{-}NH_3}$$

(A) and



$$\mathrm{CH_3\text{-}\underset{\substack{| \\ O^-}}{\overset{+}{C}}{=}NH_2}$$

(B)

as the extreme cases, hence by the hydrogen bonds the contribution of the structure (B) becomes greater in the crystal line state than in the gaseous state. As a result, C=O distance will tend to be longer and C—N distance to be shorter in the crystal.

The change in the structure of acetamide due to the formation of a hydrogen bond is supported by another fact. N-methylacetamide in dilute benzene solution shows an infrared absorption maximum of C=O vibration at 1700 cm^{-1} in extreme dilution, but its wave number shifts to 1640 cm^{-1} as the concentration increases[3] owing to the hydrogen bond between solute molecules.

Summary

1) The molecular structures of acetamide and N-methylacetamide were determined using electron diffraction by gases. The results were compared with the values obtained from X-ray diffraction by crystals.

2) C=O distance is longer in the crystalline state than in the gaseous state, while C—N distance is shorter in the crystalline state than in the gaseous state. This is due to the hydrogen bond which is absent in the gaseous state but exists in the crystalline state.

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