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Structure of *trans*-*N*-methylacetamide: planar or non-planar symmetry?

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Abstract

The structure of *trans*-*N*-methylacetamide has been fully optimized, i.e., all frequencies real, at the Hartree–Fock (HF) level with twelve basis sets from 6-31G* through 6-311++G** and with electron correlation at the second-order Møller–Plesset perturbation level (MP2) with the 6-31G*, 6-311G**, 6-31+G*, 6-311+G*, and 6-311++G** basis sets. Minimum energy structures are non-planar at HF and MP2 levels without diffuse functions. With diffuse functions included, the minimum energy structure is planar for all basis sets at the HF level and tends toward planarity at more complete levels of MP2 electron correlation. These results, as well as MP3, MP4 (SDQ), and CISD optimizations without frequency calculations, lead us to conclude that, within the expected torsion angle variations in such calculations, the equilibrium structure of the isolated molecule has planar symmetry.

1. Introduction

trans-*N*-methylacetamide (*t*-NMA) (Fig. 1) is the simplest model molecule for the peptide group in proteins, and it has therefore been studied extensively. Its structure has generally been taken to have planar symmetry, particularly since the crystal structure determination [1] indicated a *t*-NMA molecule with coplanar heavy atoms. This has also been assumed to be the case for the isolated molecule in gas-phase electron diffraction [2] and infrared spectroscopy [3] studies, although infrared spectra of *t*-NMA molecules isolated in inert gas matrices have been interpreted in terms of both planar [4] and non-planar [5] geometries. (The terms "planar" and "non-planar" will be used throughout this paper to mean planar and non-planar symmetry, respectively.)

Ab initio calculations have also been used to try to establish the geometry of the isolated *t*-NMA molecule. With a 4-21 Gaussian basis set [6], the fully optimized geometry was found to be planar, as was also true for the 3-21G basis set [7,8]. This means that all normal mode frequencies are real and the molecule is at a true potential energy minimum. However, with larger basis sets such as 4-31G* and 6-31G*, it was found [8] that the planar structure, while at a stationary point, had imaginary frequencies, i.e., negative eigenvalues, associated with the two CH_3 torsions, indicating that the planar structure was actually at a saddle point and that the true minimum energy structure was non-planar. In order to obtain the higher frequency spectrum, these two coordinates were dropped from the normal mode calculation [8]

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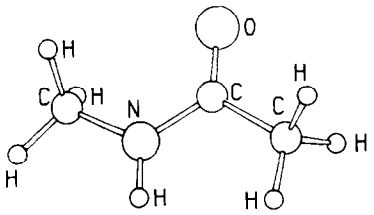

Fig. 1. Structure of *N*-methylacetamide in the conformation with (C)H cis to (N)H and (C)H trans to (C)O (conformer IV [8]).

(equivalent to assuming freely rotating CH_3 groups), as had been done by others [9,10], an assumption that was satisfactory for this purpose. The slightly lower energy non-planar structure has been noted [11], and its parameters specified for the 6-31G* basis set [12].

Since a non-planar structure implies that the *t*-NMA molecule is chiral, with the possibility of detecting this experimentally [12], it is vital that this conclusion be established with confidence. We have examined this structural question with larger basis sets, and find that the isolated *t*-NMA molecule is expected to have planar symmetry.

2. Computational details

Ab initio calculations were performed with the GAUSSIAN 92 program [13] on Cray C90 (at the San Diego Supercomputer Center), IBM RS/6000, and DEC Alpha 3000 computers.

Calculations of fully optimized structures, i.e, with all real frequencies, of *t*-NMA were performed at the Hartree–Fock (HF) level using the following valence double- and triple-split basis sets: 6-31G*, 6-31G**, 6-311G*, 6-311G**, 6-31+G*, 6-31+G**, 6-31++G*, 6-31++G**, 6-31+G(2df,2pd), 6-311+G*, 6-311+G**, 6-311++G*, 6-311++G**, and 6-311+G (2df, 2pd). In addition, we carried out calculations with electron correlation included at the second-order Møller–Plesset perturbation level, MP2, with 6-31G*, 6-311G**, 6-31+G*, 6-311+G*, and 6-311++G** basis sets. Harmonic vibrational frequencies were computed from analytical second derivatives for all the HF and MP2 optimized geometries. With the 6-31+G* basis set we also performed third- and fourth-order Møller–Plesset geometry optimizations, MP3 and MP4(SDQ), respectively. Electron correlation effects were also evaluated with the configuration interaction method, including all single and double excitations (CISD), which is based on the variational principle. Frequencies were not calculated for the MP3, MP4, and CISD optimized structures.

3. Results and discussion

Table 1 shows the fully optimized structures and total (and in some cases relative) energies of *t*-NMA obtained at the HF level with some of the basis sets used. Since we are interested in the question of planar or non-planar symmetry, only the dihedral angles of the optimized structures are shown.

At the HF/6-31G* level, the final structure of *t*-NMA depends on the starting point for the optimization. If the starting structure is planar, the final structure remains planar but is at a saddle point with respect to the (C)CH_3 torsion [8]. If the starting structure is non-planar, true minima are obtained, with a peptide group that is non-planar by $\approx 6°$, a (N)CH_3 group rotated by up to $\approx 11°$ from the (C)H cis to the (N)H position, and a (C)CH_3 group rotated by $\approx 21°$ from the (C)H trans to the (C)O position (thus corresponding to a distorted conformer IV [8]). These angles vary slightly with the starting non-planar structure even though all frequencies are still real. For example, for three equal lowest energy structures, while the peptide and (N)CH_3 torsion angles are the same, the (C)CH_3 angle differs by up to 0.4°; for five structures of equal energy but 0.001 kcal mol^{-1} higher than the minimum, variations from the angles at the minimum are up to 0.8° in the peptide group, up to 1.0° in the (N)CH_3 group, and up to 3.0° in the (C)CH_3 group; for a structure 0.003 kcal mol^{-1} higher than the minimum, the variation in the peptide group is 1.2°, that in (N)CH_3 is 0.8°, and that in (C)CH_3 is 3.2°. Optimized structures that differ by 0.002 kcal mol^{-1} can have CCH_3 dihedral angles that differ by up to 6°. Since such energy differences cannot be considered meaningful, torsion angle variations of up to $\approx 6°$ are also not significant.

Table 1
Fully optimized[a] HF structures and energies of *trans*-*N*-methylacetamide

Torsion angle	Basis set							
	6-31G*	6-311G*	6-31+G* P,N[b]	6-311+G* P,N[b]	6-31+G(2df,2pd)		6-311+G(2df,2pd)	
					P[b]	N[b]	P[b]	N[b]
OCNH	186.0	187.2	180.1	180.1	180.0	181.2	180.0	179.6
OCNC	−4.0	−4.8	0.0	0.0	0.0	−1.2	0.0	0.1
CCNH	5.3	6.7	0.1	0.1	0.0	0.7	0.0	−0.6
CNCH	168.7	164.1	179.7	179.7	179.9	178.7	179.9	180.5
CNCH	49.4	45.1	60.0	60.0	60.1	59.0	60.1	60.6
CNCH	−70.9	−75.3	−60.5	−60.5	−60.1	−61.3	−60.2	−59.7
NCCH	−99.4	−101.0	−121.9	−121.7	−121.6	−112.3	−121.5	−119.0
NCCH	21.4	19.8	−0.3	−0.1	0.1	8.9	0.1	2.4
NCCH	143.4	141.8	121.3	121.5	121.7	130.8	121.7	124.2
E[c]	.006164	.061014	.013851	.066978	.047537	.047534	.098183	.098183
ΔE[d]					(0	0.002)	(0	0)

[a] All frequencies real. [b] P, planar starting structure; N, non-planar starting structure (all dihedral angles deformed 5° or more from planar). [c] In hartrees, with −247 before decimal point. [d] In kcal mol^{-1}, with reference to the same basis set.

Increasing the size of the basis set to HF/6-311G* keeps the peptide distortion about the same, increases the NC torsion to $\approx 15°$, and reduces the CC torsion to $\approx 20°$ from planarity. While such variations produce essentially no changes in most unscaled normal mode frequencies, CC torsion and NC torsion vary by up to 15 cm^{-1}, and amide V varies by up to 25 cm^{-1}. The addition of polarization functions to the hydrogen atoms, i.e., 6-31G**, 6-311G**, yields essentially the same results.

In increasing the size of the basis set, it is probably very important to have a satisfactory representation of the electron density that is far from the core, such as in lone pairs. Addition of diffuse functions accomplishes this by giving additional flexibility to the directionality of the electron density. When we add diffuse *sp*-functions on the heavy atoms, we find that for all basis sets and independent of the starting point, the minimum-energy *t*-NMA structure has planar symmetry and is conformer IV [8] (Table 1 and Fig. 1). The other planar conformers [8] are at saddle points on the potential energy surface, with relative energies (in kcal mol^{-1}) and number of imaginary (CH_3 torsion) frequencies of II: 0.17–0.20, 1, III: 0.39–0.36, 1, and I: 0.55–0.54, 2, for 6-31+G* to 6-311++G**. Addition of diffuse *s*-functions on the hydrogen atoms has a negligible effect.

We enhanced the HF basis sets further by replacing the standard set of first polarization functions on non-hydrogen atoms by two sets of *d*-functions and a single set of *f*-functions, and on the hydrogen atoms by two sets of *p*- and one set of *d*-functions, for both 6-31+G* and 6-311+G* basis sets (Table 1). In the case of 6-31+G(2df,2pd), if the starting structure for the optimization procedure is planar so is the optimized structure. However, if we start with a deformed structure (rotating all the torsion angles out of planarity by 5° or more), the optimized structure has a (C)CH_3 group rotated by about 9°. Both structures are true minima, with negligibly different energies ($\Delta E = 0.002$ kcal mol^{-1}). With the triple zeta 6-311+G(2df,2pd), the structures obtained with these different starting points have the same absolute energy and the deformation of the (C)CH_3 has decreased to $\approx 2°$. In view of our earlier observation about the expected variability in these angles, this structure should be considered planar.

At the MP2/6-31G* level (Table 2), the peptide group becomes more nearly planar than at HF/6-

31G*, the $(N)CH_3$ group switches over to a slightly distorted (C)H trans to the (N)H position, and the $(C)CH_3$ group stays the same. At MP2/6-311G* (not shown), all groups become further distorted from planarity compared to HF/6-311G*.

In the case of electron correlation at the MP2/6-31+G* level, the final structure again depends on the starting point. If the starting structure is planar, the final structure is essentially planar and is at a saddle point. However, if the starting structure is non-planar, we get an unusual result, namely, starting from two different initial distorted structures and different force and displacement constraints, we find two different fully optimized structures of exactly the same energy with opposite peptide group ($\approx 4°$) and $(C)CH_3$ ($\approx 10°$) rotations about a $\approx 4°$ distorted $(N)CH_3$ group (see (1) and (2) of Table 2). These were frozen-core MP2 calculations, in which the inner shell is excluded from the correlation energy calculation. However, if we do a full MP2 optimization, i.e., all electrons included in the correlation, with tight convergence criteria for the maximum force and displacement, 1.5×10^{-5} and 6×10^{-5}, in a.u., respectively, the optimized structure has nearly planar ($\approx 1°$ deviation) peptide and $(N)CH_3$ groups and a $(C)CH_3$ group that deviates $\approx 4°$ from planarity (see (3) of Table 2). A similar, but slightly more planar, structure was obtained with extra tight force and displacements constraints, up to 1×10^{-7} and 1×10^{-6} in a.u., respectively (see (4) of Table 2). Furthermore, starting from a planar structure, tight and full optimizations give essentially planar structures, i.e. 0.1° amide non-planarity, 1.5° $(C)CH_3$ rotation, having exactly the same absolute energy as (3) but with a saddle point. We also note that, with the same starting point as that of (3) but without full MP2 optimization, the resulting structure has about the same $(C)CH_3$ rotation and is $\approx 1°$ more non-planar with respect to the peptide and $(N)CH_3$ groups, but is at a saddle point with an energy of 0.001 kcal mol^{-1} higher (not shown).

Geometry optimizations at the MP3/6-31+G* level (Table 3) yield results that are similar to those at MP2/6-31+G*, except in this case the

Table 2
Fully optimized[a] MP2 structures and energies of *trans*-*N*-methylacetamide

Torsion angle	Basis set				
	MP2/6-31G*	MP2/6-31+G*			
		(1)[b]	(2)[c]	(3)[d]	(4)[e]
OCNH	181.7	175.6	184.3	181.1	181.0
OCNC	−1.5	3.0	−2.9	−0.8	−0.7
CCNH	0.1	−4.1	4.1	0.9	0.8
CNCH	126.5	176.1	176.1	179.0	179.1
CNCH	7.3	56.5	56.4	59.0	59.1
CNCH	−111.8	−63.3	−63.4	−60.7	−60.6
NCCH	−99.4	−131.2	−112.5	−117.7	118.1
NCCH	21.8	−9.6	8.9	3.8	3.5
NCCH	143.3	111.8	130.5	125.4	125.0
E[f]	.729533	.747753	.747753	.769319	.769319
ΔE[g]		(0	0)	(0	0)

[a] All frequencies real. [b] Starting from conformer III [8] with 10° CH_3 group rotations. Default force (4×10^{-4} a.u.) and displacement (1.8×10^{-3} a.u.) constraints. [c] Starting from conformer IV [8] with 2° peptide and 10° CH_3 group rotations. Tight force (1.5×10^{-5} a.u.) and displacement (6×10^{-5} a.u.) constraints. [d] Starting from conformer IV [8] with 5° or more peptide and CH_3 group rotations. Tight force (1.5×10^{-5} a.u.) and displacement (6×10^{-5} a.u.) constraints. Correlation extended to core electrons. [e] Starting from conformer IV [8] with 5° peptide and CH_3 group rotations. Extra tight force (1×10^{-7} a.u.) and displacement (1×10^{-6} a.u.) constraints. Correlation extended to core electrons. [f] In hartrees, with −247 before decimal point. [g] In kcal mol^{-1}, with reference to the same basis set.

planar structure has the lowest energy. The slightly deformed structure has a planar peptide group and both CH_3 groups rotated by $\approx 5°$ from planarity. Fourth-order Møller–Plesset optimizations, MP4(SDQ)/6-31+G*, including all single, double and quadruple substitutions (omitting triple substitutions), give results similar to the above, except in this case the slightly deformed structure has the lower energy (by ≈ 0.006 kcal mol^{-1}) and the peptide group has a $\approx 3°$ deformation. At the CISD level, the planar and deformed optimized geometries differ in energy by 0.001 kcal mol^{-1}, with the slightly higher absolute energy non-planar structure having a (C)CH_3 group deformed from planar symmetry by $\approx 8°$. We should note that, although frequencies were not calculated in these cases, in all other such situations the lowest energy structure was never at a saddle point.

In order to relate the energy differences between minima and saddle points to other properties of the potential surface, we have calculated barriers between minima and zero-point energies for the CH_3 torsions. At the MP2 level, such barriers are of the order of 0.005 kcal mol^{-1}. The zero-point energies, calculated from scaled HF/6-31+G* force constants, are ≈ 0.040 kcal mol^{-1} for the (C)CH_3 torsion and ≈ 0.100 kcal mol^{-1} for the (N)CH_3 torsion.

What do these results say about the structure of the isolated *t*-NMA molecule? Firstly, they indicate that any conclusion about planarity is unusually basis-set-dependent. At the HF level, addition of diffuse functions, which would seem to be minimally necessary, clearly produces a planar structure. Introduction of electron correlation results in departures from planarity, but such departures are very sensitive to the starting structure and diminish as core electron correlation and tighter force and displacement constraints are included. Secondly, as already noted [8], the potential surfaces for the CH_3 torsions are ill-defined and, as we have seen, have multiple shallow minima and saddle points. This situation is similar to the case of formamide, which was inferred to have a very shallow potential with respect to CH_3 torsions and for which "the deviation from planarity of the molecule [is] so small that this species should be considered as a planar system" [14]. Thirdly, since the zero-point energies for the CH_3 torsions are an order of magnitude larger than the barriers between stationary states, it is reasonable to conclude, as in the similar cases of 2-aminoethanol and *N*-formylproline amide [15], that

Table 3
Optimized[a] MP3, MP4, and CISD structures and energies of *trans*-*N*-methylacetamide

Torsion angle	Basis set					
	MP3/6-31+G*		MP4/6-31+G*		CISD/6-31+G*	
	P[b]	N[b]	P[b]	N[b]	P[b]	N[b]
OCNH	180.1	180.8	180.1	184.2	180.0	181.4
OCNC	0.0	−0.6	−0.2	−2.6	0.0	−1.2
CCNH	0.1	0.5	0.1	4.4	0.0	1.0
CNCH	179.9	174.9	179.9	174.8	179.9	178.4
CNCH	60.0	55.1	59.9	55.2	60.0	58.6
CNCH	−60.0	−64.8	−59.9	−64.8	−60.1	−61.5
NCCH	−121.5	−116.5	−121.4	−116.5	−121.5	−113.8
NCCH	0.0	4.9	0.0	5.0	0.1	7.6
NCCH	121.5	126.4	121.4	126.5	121.7	129.3
E[c]	.771945	.771941	.787464	.787474	.660077	.660076
ΔE[d]	(0	0.003)	(0.006	0)	(0	0.001)

[a] No frequency calculations performed. [b] P, planar starting structure; N, non-planar starting structure (all dihedral angles deformed 5° or more). [c] In hartrees with −247 preceding decimal point. [d] In kcal mol^{-1}, with reference to the same basis set.

"these shallow minima can be considered to be physically meaningless."

Thus, isolated *t*-NMA has, within the expected torsion angle variations of our HF and MP ab initio calculations, a planar symmetric structure. This structure can probably undergo small librational type fluctuations associated with the flat CH_3 potentials and the "coupling" of CH_3 and peptide group rotations. Finally, we note that the introduction of interactions such as hydrogen bonding to the CO and NH groups stabilizes the planar structure [16].

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