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N-Benzylformamide at 150 K

Anna Michta,[a]* Maria Nowak[b] and Joachim Kusz[b]

[a]Institute of Chemistry, University of Silesia, 14 Bankowa Street, 40-006 Katowice, Poland, and [b]Institute of Physics, University of Silesia, 4 Uniwersytecka Street, 40-007 Katowice, Poland
Correspondence e-mail: anna.michta@us.edu.pl

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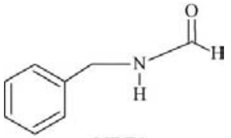
The title compound, C_8H_9NO, crystallizes with $Z' = 2$. Each type of independent molecule links into a separate N—H···O hydrogen-bonded chain in the *a*-axis direction. There are also three weak C—H···O hydrogen bonds, which join the molecules into a two-dimensional sheet parallel to (001). The molecules exhibit the *trans* conformation of the –NHCHO group and an *anti* conformation around the (Ph)C—NH(CHO) bond. The formamide group in each of the symmetry-independent molecules is twisted out of the benzyl group plane, forming angles of 75.96 (10) and 65.23 (11)° with this plane. The significance of this study lies in the comparison drawn between the experimental and calculated data of the crystal structure of the title compound and the data of several other derivatives possessing the $-CH_2-NH-CO-$ group. The correlation between the IR spectrum of this compound and the hydrogen-bond energy is also discussed. This molecular system is of particular interest to biochemists because of its preventative function against toxic products of alcohols in human metabolism.

Comment

Monosubstituted formamides are good inhibitors of class I (α, β and γ) and class II (π) human alcohol dehydrogenase (HsADH; Schindler *et al.*, 1998). *N*-Benzylamides have anticonvulsant functions (Kushner *et al.*, 1951; Malawska *et al.*, 2004). The title compound, *N*-benzylformamide (NBFA), is the simplest *N*-benzylamide and thus its biological function has attracted considerable interest in recent years. NBFA is a selective inhibitor for the HsADH $\beta1$ enzyme (Schindler *et al.*, 1998). The structure of the HsADH $\beta(1)\beta(1)$ isoform complexed with NBFA was determined by X-ray methods with 1.6 Å resolution (Gibbons & Hurley, 2004). The novel enzyme *N*-substituted formamide deformylase (NfdA) was discovered in the microorganism *Arthrobacter pascens* F164, which was able to grow on NBFA as a sole nitrogen source (Fukatsu *et al.*, 2005). The gene (NfdA) encoding this enzyme was also cloned (Fukatsu *et al.*, 2004). NBFA is of great importance for the reduction with $NaBH_4$ to benzylmethylamine (Zhu *et al.*, 2003). The conformational analysis of NBFA was performed with the help of density functional theory and second-order Møller–Plesset (MP2) calculations (Vargas *et al.*, 2001; Robertson *et al.*, 2000). The dielectric properties and the self-association process of NBFA solutions in carbon tetrachloride have been studied on the basis of IR spectroscopy (Jadżyn *et al.*, 1986).


NBFA

The objects of our research are the IR spectra of the secondary amide crystals in the frequency range of the proton and deuteron stretching vibrations in the hydrogen bond (Flakus & Michta, 2008). Characteristic isotopic and spectroscopic effects, called the self-organization effect, are observed in this vibration frequency range (Flakus, 1989, 2003; Flakus & Bańczyk, 1999). Measurements of the polarized IR spectra of spatially oriented diverse hydrogen-bond systems present in the lattices of molecular crystals allow us to estimate the polarization properties of transitions found in the excited states of the proton vibrations in the crystals; these transitions contribute to the ν_{X-H} band generation mechanisms in the crystalline spectra. Thus, for the reliable interpretation of the self-organization mechanism, the crystal structure of the hydrogen-bond system must be known. In the case of NBFA, a crystallographic study has not yet been reported.

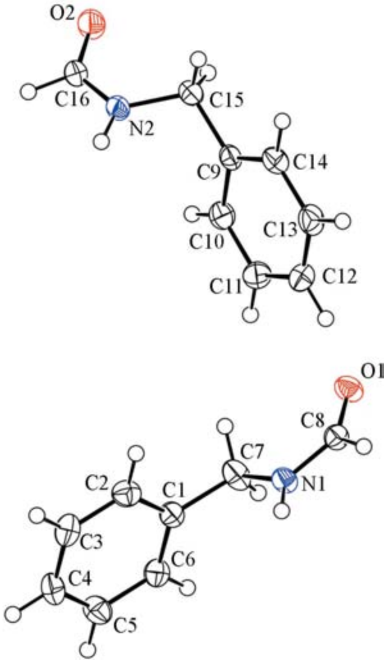


Figure 1
The two symmetry-independent molecules of NBFA, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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In this article, the results of our structural studies of the hydrogen bonds of NBFA are presented. NBFA crystallizes with two molecules in the asymmetric unit (Fig. 1), which exhibit comparable bond lengths and angles. In both molecules, the –NHCHO group adopts a *trans* conformation, with deviations from planarity smaller than 1°, and the conformation around the (Ph)C—N(CHO) bond is *anti* (the *syn* conformation of the PhC—NH group). The *trans* arrangement of the NH—CO group is more frequently found in nature than the *cis* form (Galabov *et al.*, 2003). The calculated energy for the *cis* form of NBFA is about 7.6 kJ mol^{-1} higher than that calculated for the *trans* isomer (Robertson *et al.*, 2000). Thus the *trans* conformation of the NH—CO group is more stable than the *cis* one.

The formamide group is twisted out of the benzyl group plane, and the angles between this plane and the amide group plane are 75.96 (10) and 65.23 (11)° for the symmetry-independent molecules containing atoms N1 and N2, respectively. The largest deviations from the least-squares benzene plane are observed for atoms C2 (C10) and C4 (C12), and the deviations are in the range 0.0047–0.0124 Å. The C(H$_2$)—N and C=O bond lengths are in the region of 1.460 and 1.232 Å, respectively, and compare well with those of related compounds, such as butanediyldiformamide (Chaney *et al.*, 1996), *N*,*N*′-dibenzyloxalamide (Nieger *et al.*, 2001) or (*R*)-*N*-benzylmandelamide (Salas-Coronado *et al.*, 2001). These bond lengths are also in good agreement with those calculated by the MP2/DZP and MM3 methods (Vargas *et al.*, 2001). The length of the N—C(=O) bond is slightly shorter (1.324 Å) than the calculated value but is in good agreement with those of related compounds, such as (*R*)-*N*-benzylmandelamide (Salas-Coronado *et al.*, 2001), *N*-formylglycine (Görbitz & Sagstuen, 2004) or 1-formylamino-2-(2-hydroxyphenyl)-1-phenylethylene (Viossat *et al.*, 1986). The main differences between the calculated and the experimental values are observed for two torsion angles, namely C2—C1—C7—N1 (C10—C9—C15—N2) and C1—C7—N1—C8 (C9—C15—N2—C16). For the N1-containing molecule, the experimental angles are 68.50 (15) and −162.61 (12)°, respectively, and for the other molecule they are 51.60 (15) and −149.33 (12)°. The values of these angles calculated by the MP2/DZP method were 106.4 and −83.4° (Vargas *et al.*, 2001) and by the MP2/6–31G** method were 71 and −92° (Robertson *et al.*, 2000). In related compounds, these two torsion angles can adopt values that are significantly different from one another, *e.g.* in *N*-{[3′-formyl-2,2′-bis(methoxymethoxy)biphenyl-3-yl]methyl}-formamide (76.46 and −105.78°; Gao *et al.*, 2006) or *N*-acetylbenzamide (21.79 and −166.23°; Etter *et al.*, 1991).

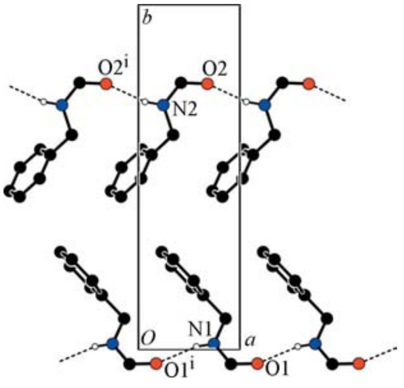

Figure 2
A view along the *c* axis of the N—H···O hydrogen-bonded chains of NBFA molecules. [Symmetry code: (i) $x - 1, y, z$.]

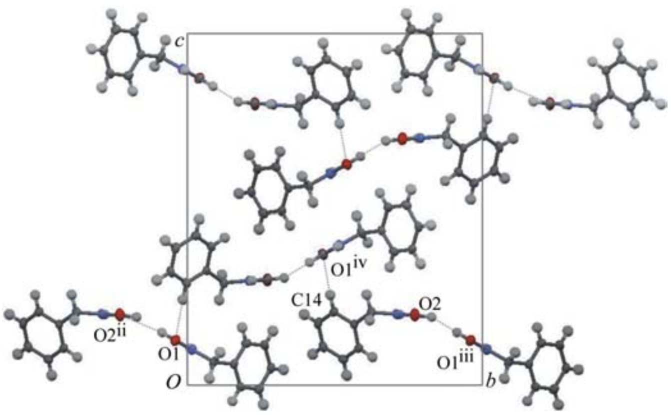

Figure 3
A view along the *a* axis, showing weak C—H···O hydrogen bonds. Atoms C8 and C16 are wholly obscured behind O1 and O2, respectively. [Symmetry codes: (ii) $x, y - 1, z$; (iii) $x - 1, y + 1, z$; (iv) $-x + \frac{3}{2}, y + \frac{1}{2}, -z + \frac{1}{2}$.]

A search of the Cambridge Structural Database [CSD, Version 5.28 (Allen, 2002); *ConQuest*, Version 1.9 (Bruno *et al.*, 2002)] for other NBFA derivatives yielded only two very complex structures, namely *N*-{[3′-formyl-2,2′-bis(methoxymethoxy)biphenyl-3-yl]methyl}formamide (Gao *et al.*, 2006) and *catena*-[(μ_3-4-{*N*-formyl-*N*-[methylene(phosphonato)]-ammoniomethyl}benzoate)-(μ_2-4-{*N*-formyl-*N*-[methylene-(hydrogenphosphonato)]ammoniomethyl}benzoate)aquaerbium(III)] (Tang *et al.*, 2006). Substitution at the phenyl and amino groups exerts strong and complex effects on the geometry of both molecules, making them unsuitable for comparison with NBFA.

In the crystal structure of NBFA, the two symmetry-independent molecules interact *via* N—H···O hydrogen bonds (Table 1), forming two separate extended zigzag chains parallel to the *a* axis with graph-set notation $C_1^1(4)$ (Fig. 2; Bernstein *et al.*, 1990; Grell *et al.*, 1999). There are also three weak C—H···O hydrogen bonds (Table 1) with graph-set notation $D_1^1(2)$ (Bernstein *et al.*, 1990; Grell *et al.*, 1999). These bonds join the molecules into a two-dimensional network parallel to (001) (Fig. 3). The second-level graph-set notation gives about 17 possible arrangements of the hydrogen-bond rings, for example, $R_3^2(8)$ and $R_4^3(12)$ (Fig. 4; Bernstein *et al.*, 1990; Grell *et al.*, 1999).

The values of the N—H···O hydrogen-bond distances are in the range 2.5–3.2 Å and therefore they can be regarded as strong hydrogen bonds (Desiraju & Steiner, 1999). The strength of the hydrogen bonds in this compound was also investigated with IR spectroscopy. The band of the isolated N—H stretching vibration, $\nu_{\rm N-H}$, is located at a frequency of 3400 cm^{-1}. In the case of NBFA, we observed the band of the

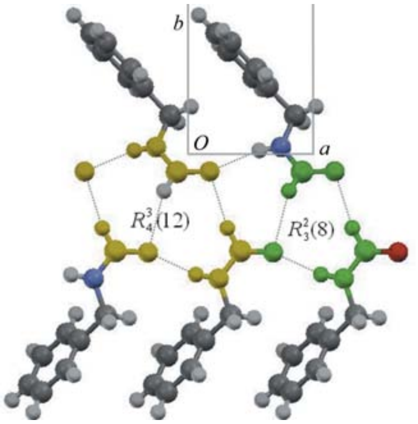

Figure 4
A view along the *c* axis, showing the formation of $R_3^2(8)$ and $R_4^3(12)$ rings. (In the electronic version of the paper, the atoms comprising these motifs are shown in green and yellow, respectively.)

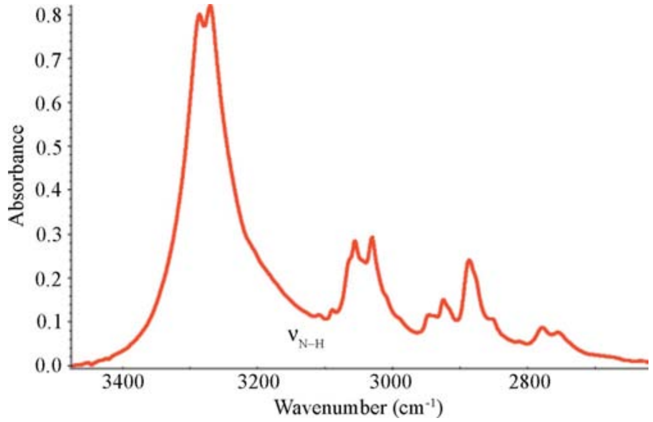

Figure 5
The IR spectrum of NBFA measured by the KBr pellet technique at room temperature, showing the ν_{N-H} frequency range.

N—H stretching vibration in the frequency range 3350–2800 cm^{-1}, with a shift of about 300 cm^{-1} (Fig. 5). This relative shift is larger than 5% and this value is characteristic of a strong hydrogen bond (Desiraju & Steiner, 1999).

Experimental

NBFA was purchased from Sigma–Aldrich and used without further purification. It was dissolved in an acetone–petroleum ether mixture (1:1 *v*/*v*). After several days, colorless single crystals of NBFA had formed, which proved to be suitable for single-crystal X-ray diffraction analysis.

Crystal data

C_8H_9NO
$M_r = 135.16$
Monoclinic, $P2_1/n$
$a = 4.7069$ (9) Å
$b = 16.036$ (3) Å
$c = 19.104$ (4) Å
$\beta = 91.08$ (3)°
$V = 1441.7$ (5) Å^3
$Z = 8$
Mo $K\alpha$ radiation
$\mu = 0.08$ mm^{-1}
$T = 150$ (2) K
0.5 × 0.13 × 0.10 mm

Data collection

Oxford Diffraction diffractometer with Sapphire3 CCD detector
16700 measured reflections
5660 independent reflections
3204 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.062$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.066$
$wR(F^2) = 0.142$
$S = 1.00$
5660 reflections
197 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\rm max} = 0.39$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.51$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O1^{i}	0.833 (14)	2.079 (15)	2.8913 (14)	164.5 (14)
N2—H2N···O2^{i}	0.867 (14)	1.990 (14)	2.8370 (14)	165.2 (13)
C8—H8···O2^{ii}	0.965 (14)	2.554 (14)	3.4831 (16)	161.7 (11)
C16—H16···O1^{iii}	0.997 (14)	2.547 (14)	3.4601 (16)	152.2 (11)
C14—H14···O1^{iv}	0.976 (16)	2.508 (16)	3.4718 (18)	169.4 (11)

Symmetry codes: (i) $x-1, y, z$; (ii) $x, y-1, z$; (iii) $x-1, y+1, z$; (iv) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$.

The aromatic and methylene H atoms were treated as riding on their parent atoms, with C—H = 0.95 and 0.99 Å, respectively. H atoms involved in hydrogen bonding were located in a difference Fourier map and their positional parameters were refined freely (refined bond lengths are given in Table 1). For all H atoms, $U_{\rm iso}$(H) values were taken as 1.2 times $U_{\rm eq}$(C,N).

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2008).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3271). Services for accessing these data are described at the back of the journal.

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