Formyl C−H···O Hydrogen Bonding in Crystalline Bis-Formamides?

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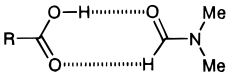
Received February 27, 1996

Although chemists normally consider the formyl hydrogen in aldehydes, formates, and formamides to be almost neutral or slightly hydridic,[1,2] recent crystallographic studies[3,4] of two DMF complexes of carboxylic acids have highlighted the presence of short contacts between the formyl hydrogen of DMF and the carbonyl oxygen of the acid. After excluding formyl groups



"locked" with their hydrogens within van der Waals contact of an oxygen acceptor, our own search of the Cambridge Structural Database (CSD)[5,6] revealed 48 formamide and 64 other formyl C−H···O contacts with H···O distances less than 2.5 Å.[7] Recent high-level *ab initio* calculations[8] suggest that the C−H···O interaction contributes 2−3 kcal mol^{-1} toward the stabilization energy of acid−formamide dimers, even when the H···O distance is as large as 2.43 Å. Nevertheless, the preponderance of longer formyl C−H···O contacts in many structures suggest that observations of short formyl C−H···O contacts are often secondary consequences of stronger interactions in the crystal. Here we show that this C−H···O interaction can be an important factor controlling the crystal structures of simple bis-formamides, but we also present spectroscopic and computational evidence that it should not be considered a conventional H-bond.[9,10]

In our molecular recognition studies of formyl groups, we noticed that bis-formamides of the formula $HCO(NH)(CH_2)_n(NH)OCH$ ($n = 4−7$) show a striking (35 °C) melting point alternation for odd and even chains (Figure 1).[11] Structural models suggest that this large alternation arises from the complementary arrangement of amide N−H···O═C H-bonds in crystals of even-chain bis-formamides (Figure 2), and its absence in the odd-chain crystals (which we have been unable to grow for X-ray diffraction studies).[12] Anomalous melting points for $n = 2$ and 8 suggested that at least three different types of packing arrangements should be accessible in the even-chain series, as confirmed by our structures of ethanediyldifor-

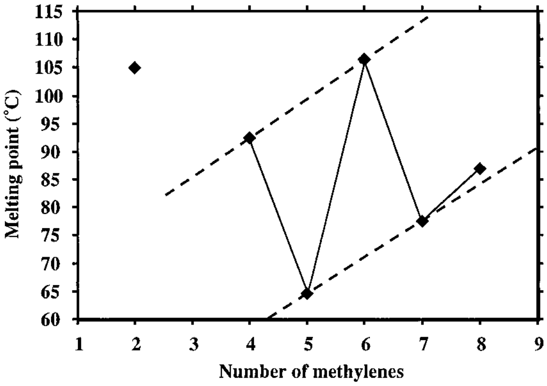


Figure 1. Melting point vs methylene chain length for alkanediyldiformamides. The 35 °C alternation for $n = 4−7$ (dashed lines) highlights the difference in H-bonding complementary for the even and odd chains. Melting points (°C) are 2:105, 4:92.5, 5:64.5,[11] 6:106.5, 7:77.5,[11] 8:87 (for *n*: mp).

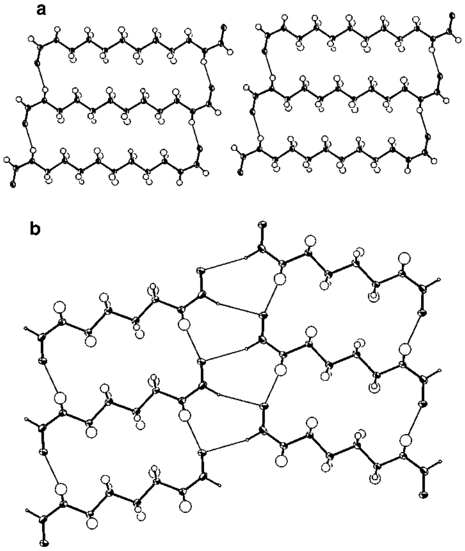


Figure 2. ORTEP packing diagrams showing (a) the $\bar{1}$ motif for antiparallel ribbons that form a layer of ODDF ([001] vertical) and (b) the 2_1 layer motif for BDDF ([010] vertical). Selected intra- and intermolecular distances (Å) and angles (deg) for the formyl−formyl interactions are given here: BDDF C−H 0.96(3), C···O 3.378(5), H···O 2.44(3), C−H···O 166(3), C−O···H 102.8(8); ODDF C−H 0.96(3), C···O 3.345(3), H···O 2.60(3), C−H···O 135(2), C−O···H 101.1(6). With normalized C−H bonds (1.083 Å), the H···O distances would be 2.32 Å in BDDF, 2.34 Å in HDDF at (22 °C), and 2.52 Å in ODDF.

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(7) Formyl C−H bonds were normalized to the standard neutron length (1.083 Å) before these searches, which excluded substructures containing metals bound to the formyl oxygen. H···O contacts as short as 2.20 Å were observed.

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(12) Except for the 1:1 complex of cytosine and *N*-formylglycine,[13] organic structures containing the $HCO(NH)CH_2$- linkage are conspicuously absent from the CSD. Well aware that impurities inhibit crystal growth, we surmised that growth of the *Z* form of primary *N*-alkylformamides would be impaired by the high concentration of the *E* isomer,[14] which constitutes up to 20% of the mixture in a number of solvents and interconverts with the *Z* isomer slowly. Our survey of *N*-alkylformamides in a variety of solvents showed that DMSO gives a high (97:3) *Z*/*E* ratio at 22 °C (by ^1H NMR in DMSO-d_6) and that it is the only suitable recrystallization solvent we have found for these bis-formamides.

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S0002-7863(96)00637-3 CCC: $12.00

mamide (EDDF), butanediyldiformamide (BDDF),[15] hexanediyldiformamide (HDDF),[16] and octanediyldiformamide (ODDF).[17] Although the 3-D network structure of EDDF cannot be compared readily with the others, the three higher homologues pack in two classes of layered structures in which ribbons of H-bonded amides are tethered by formyl groups. In ODDF, formyl dimers adopt a centrosymmetric ($\bar{1}$) motif that holds the ribbons within van der Waals contact (Figure 2a), whereas in BDDF and HDDF the formyl groups show almost identical short C−H···O contacts along a 2_1 axis relating adjacent ribbons (Figure 2b).[18]

Because the packing efficiencies of BDDF, HDDF, and ODDF are so similar[19] and the energetics of these short C−H···O contacts so poorly understood, it is currently not possible to pinpoint the forces responsible for the switch from 2_1 to $\bar{1}$ packing arrangements upon homologation. To assess both intra- and interlayer interactions reliably, lattice energy calculations utilizing accurate electrostatic multipoles are required, but the layered formamide crystals diffract poorly at high angle, so the use of electron density difference maps is infeasible. In order to better understand the nature of the C−H···O interactions in the 2_1 and $\bar{1}$ packing arrangements, and to find out specifically if the short C−H···O contacts in the 2_1 motif constitute H-bonds, we turned to infrared spectroscopy. In principle, the infrared stretching frequencies of the formyl C−H group should be indicative of H-bonding, but this spectral region is complicated by a nearby C−H bending overtone[20] and by intermolecular vibrational coupling (Davydov coupling). (The latter is a widespread (but poorly recognized) phenomenon that complicates the interpretation of solid state IR spectral shifts in terms of specific interactions.) Spectra of crystalline bis-formamides in KBr show a multitude of bands in the formyl C−H stretching region and actually show more similarities between ODDF and HDDF than between BDDF and HDDF (Figure 3a−c)![21] To circumvent problems from vibrational coupling, we grew bis-formamide crystals incorporating small amounts (3−20%) of formyl-deuterated guests in unlabeled hosts. (Dilution of the C−D chromophore is required to break up the perturbations from resonant coupling between nearest neighbors). At modest isotopic dilutions (10−20 % D), bands arising from vibrational coupling C−D stretches with nearest neighbors appear 90−116 cm^{-1} higher than the unperturbed fundamental,[22,23] but at higher dilution (3%), peaks due to coupling disappear as the fundamental from isolated formyl C−D groups appears as a single peak in the spectrum for each compound (Figure 3d−f). The small shifts (3−4 cm^{-1}) to *higher* frequencies for dilute C−D stretches in BDDF and HDDF are reliable and show that the short C−H···O contacts *stiffen* the C−H bond.

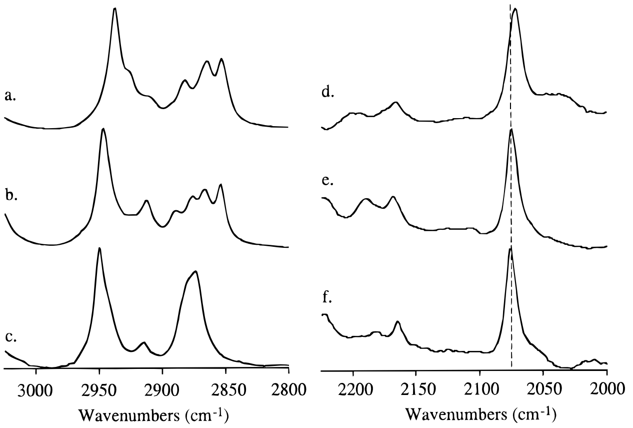

Figure 3. Infrared absorbance spectra (KBr pellets, 2 cm^{-1} resolution) of C−H stretching regions of (a) ODDF, (b) HDDF, and (c) BDDF and C−D stretching regions of (d) 3% ODDF-d_2 in ODDF, (e) 3% HDDF-d_2 in HDDF, and (f) 3% BDDF-d_2 in BDDF. Isolated C−D stretching frequencies (cm^{-1}) in d−f are 2071 (ODDF), 2074 (HDDF), and 2075 (BDDF).

If one accepts the criterion that an H-bond is accompanied by a red shift in the X−H stretching band,[10,24] this interaction cannot be considered a conventional H-bond that is stabilized by electrostatic interactions between the acceptor and a proton bound to an electronegative atom. Because the hydrogen is either neutral or slightly hydridic in isolated formyl groups,[1,2] the short C−H···O contact might arise primarily from electrostatic interactions between the carbonyl carbon and the carbonyl oxygen. To the extent that H-bonding is involved, the hydrogen should be polarized,[25] but our periodic *ab initio* calculations using CRYSTAL92 (6-31G**)[26] reveal that the difference in Mulliken populations of formyl hydrogens in 2_1 and $\bar{1}$ motifs is less than 0.3%, even though the normalized H···O distances differ by 0.2 Å. Since the C−H bond lengths are not known, this is a crude measure of polarization, but this difference seems too small for the 2_1 interaction to be considered a conventional H-bond. Our difference density studies of strongly diffracting crystals of EDDF (which also shows short C−H···O contacts) should provide a clearer picture of the electrostatic properties of this interaction.

Acknowledgment. We thank Prof. E. R. Davidson for his help with CRYSTAL92. Donors of the PRF, administered by the ACS (29932-AC4), NSERC (Canada), the Alfred P. Sloan Foundation, and the NSF (CHE-9423726) are thanked for financial support.

Supporting Information Available: Sample preparation and characterization, X-ray data collection and structure solution procedures, AGDPs, bond distances and angles, and selected least squares planes for BDDF, HDDF, and ODDF (44 pages). See any current masthead page for ordering and Internet access instructions.

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[15] $C_6H_{12}N_2O_2$, $P2_1/n$; $a = 5.645(6)$, $b = 4.687(7)$, $c = 13.620(7)$ Å; $\beta = 96.80(8)°$; $Z = 2$, $V = 357.8(7)$ Å^3 at −172 °C; $R_F = 0.053$, $R_{WF} = 0.086$, GOF = 2.60.

[16] $C_8H_{16}N_2O_2$, $P2_1/n$; $a = 8.06(5)$, $b = 4.74(4)$, $c = 12.50(7)$ Å; $\beta = 93.3(7)°$, $Z = 2$, $V = 477(5)$ Å^3 at 22 °C; $R_F = 0.060$, $R_{WF} = 0.055$, GOF = 3.25.

[17] $C_{10}H_{20}N_2O_2$, $P\bar{1}$; $a = 5.464(1)$, $b = 10.749(3)$, $c = 4.689(1)$ Å; $\alpha = 91.78(2)°$, $\beta = 94.38(2)°$, $\gamma = 101.17(2)°$, $Z = 1$, $V = 269.3(2)$ Å^3 at −162 °C; $R_F = 0.056$, $R_{WF} = 0.072$, GOF = 3.195.

[18] The structure of EDDF also contains short formyl C−H···O contacts and a twisted chain conformation that allows their occurrence. This structure will be reported elsewhere.

[19] See: Hollingsworth, M. D.; Brown, M. E.; Santarsiero, B. D.; Huffman, J. C.; Goss, C. R. *Chem. Mater*. **1994**, *6*, 1227−1244.

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[21] After an exhaustive search for polymorphism, we conclude that the structures shown here represent the bulk properties of these samples.

[22] In KBr pellets of pure formyl-deuterated ODDF (ODDF-d_2), no bands occur near 2071 cm^{-1}, but strong bands (perturbed by vibrational coupling) appear from 2193 to 2166 cm^{-1}.

[23] The three crystals show similar shifts; therefore, the intermolecular coupling probably occurs largely within an amide ribbon, with the N−H···O interaction providing the off-diagonal matrix element. (The Raman frequency of the external mode in H-bonded amides is 100−115 cm^{-1}. See: Nielsen, O. F.; Christensen, D. H.; Rasmussen, O. H. *J. Mol. Struct*. **1991**, *242*, 273−282.)

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