

Molecular Electrostatic Potentials of Hydrogen-Bonded Systems: The Oligomers of Formamide

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The modifications of the electrostatic molecular potential of formamide upon hydrogen bonding into various dimers and oligomers are presented and the predictive value of these potentials for assessing the strength of further hydrogen bonding is discussed. The potentials of long linear chains allow an understanding of the disposition of the molecules in the crystal.

Key words: Molecular electrostatic potential – Oligomers – Formamide – Hydrogen bonds.

1. Introduction

A recent Symposium [1] has stressed the role played by the molecular electrostatic potential [2] in the determination of numerous properties. While, however, the electrostatic potential of isolated molecules has been object of numerous studies, relatively little consideration has been paid to the potential of molecular complexes although the interest of the perturbation brought about by complexation on the individual potentials of the partners is evident.

We have considered recently the influence of hydrogen bonding on the molecular electrostatic potential of the proton-donor and proton-acceptor molecules [3] for a few examples. We present here complementary data based on the molecular potentials computed for various hydrogen-bonded oligomers of formamide.

From the point of view of hydrogen bonding, formamide presents a particular interest due to its ability to act as a proton-donor through either one (or both) of its NH bonds or (and) as a proton-acceptor through its carbonyl oxygen. Furthermore the disposition of these sites in the molecule makes it apt to hydrogen-bond in different fashions so as to form various linear and cyclic dimers as well as chain or mixed oligomers [4–7]. These different hydrogen-bonded structures provide a good opportunity to study the modifications brought about by hydrogen bonding in various ways on the molecular potential of the parent molecule and to characterize the transmission of the effects along chains of donor-acceptor molecules. The occurrence of such long chains of hydrogen-bonded peptide bonds in the secondary structure of proteins (either α -helical or pleated-sheet) adds to the interest for the knowledge of these effects.

The wave functions utilized to compute the molecular potentials are those of Refs. [6, 7] and correspond to an STO 3G basis set [8] like that utilized in Ref. [3].

2. Results and Discussion

2.1. Formamide and Its Dimers

Fig. 1(a to d) reproduces the molecular potentials of formamide (a), of its most stable linear dimer (b), of the end oxygen region in the same dimer with a rotation of 180° of the proton donor about the hydrogen bond axis (c), and of the oxygen region in the cyclic dimer (d). The rotated linear dimer is interesting in that it differs very little in energy from the zero rotamer ($-\Delta E = 8.21$ kcal/mole instead of 8.28). Such a facile roatation about the hydrogen bond axis in formamide dimers was noted some time ago [9] in structures where the NH...O—C bonds are aligned: the fact that it is true also in angular dimers adds interest to the knowledge of the variations of the potentials accompanying the rotation.

As observed earlier in computations with other basis sets [10], formamide presents a wide negative potential zone around the carbonyl oxygen with a small anisotropy in favour of the side of the CH bond. Two minima are observed, one on each side of the oxygen, O_i on the CH side being three kcal/mole deeper than O_e on the exterior side. (In the computations of Ref. [10] only the *minimum minimorum* was given, but the second minimum was equally present).

In the positive region, a clear non-equivalence of the NH directions appears, with the *trans* proton (*trans* to C=O) more repulsive than the *cis* proton for a positive point charge (or more attractive for a negative charge). Worth noting is the fact that the STO 3G gross atomic population computed [6] for the *trans* proton is 0.786 e against a value of 0.773 e for the *cis* proton, indicating a *less* positive character of the *trans* proton as measured by net charges. This shows once again how erroneous it may be to use net charges alone as a measure of the attractive or repulsive character of an atom for a reactant.

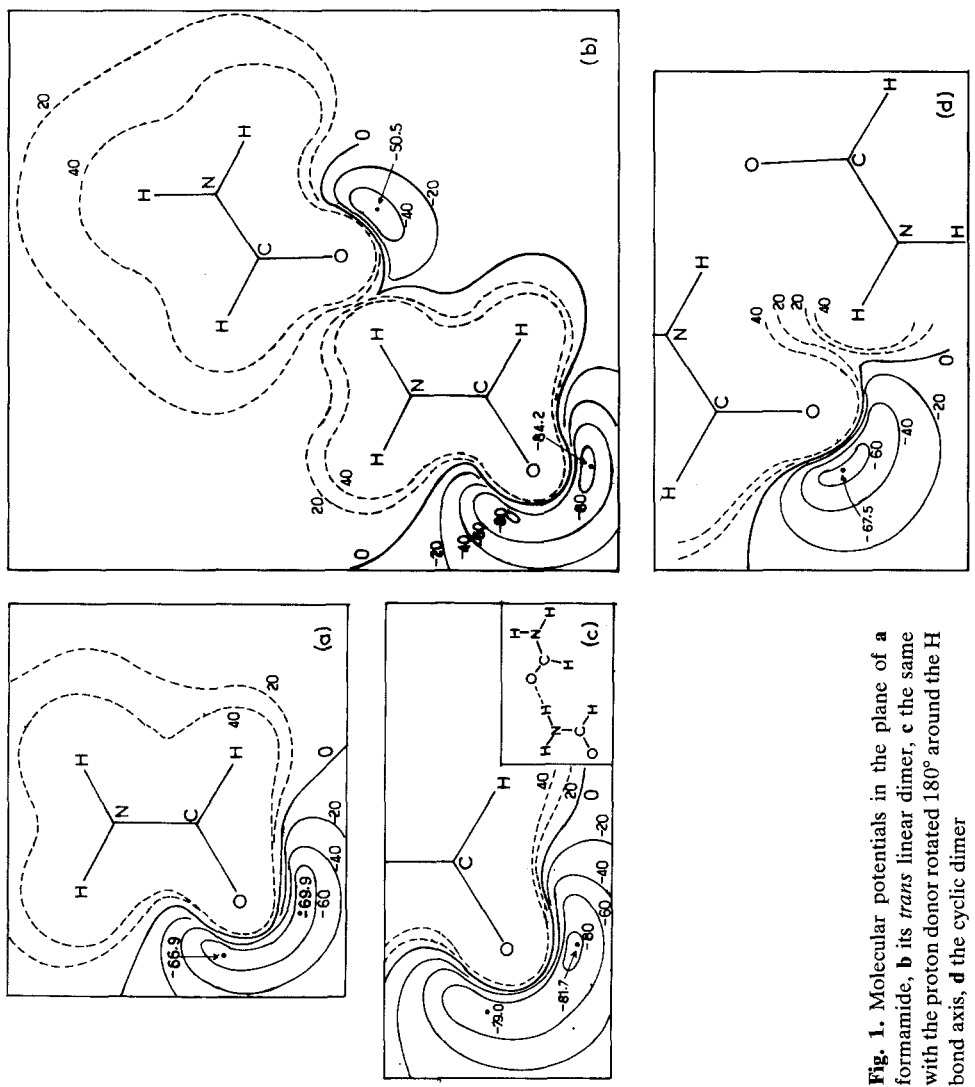


Fig. 1. Molecular potentials in the plane of a formamide, **b** its *trans* linear dimer, **c** the same with the proton donor rotated 180° around the H bond axis, **d** the cyclic dimer

Upon formation of the *trans* linear dimer it is observed that the characteristics of the molecular potential at the two extreme ends of the supermolecule conserve the same qualitative character as in the monomer, namely two separate minima in a wide negative region surrounding the end carbonyl oxygen, with a dissymmetry in favour of the CH side, strong positive potential outside the end NH₂ group with a dissymmetry in favor of NH *trans*, as in the monomer, here again in contradiction with what would be predicted by the electron populations (0.762 and 0.775 e for *cis* and *trans* protons, respectively [6]).

Aside from the qualitative similarity in the distribution of the end potentials in the monomer and linear dimer one observes an appreciable increase in their numerical values upon hydrogen bonding. As was shown in Ref. [3], this enhancement is due for one part to the polarization + charge-transfer effect of one molecule on the electron distribution of its partner, and for the other part to the pure superposition of the individual potentials of the two molecules in the region of interest: thus when in the dimer the proton acceptor is oriented so that its negative region extends into the negative region of its partner, enhancement of the attraction occurs by simple superposition. In the water dimer, with the same basis set, this addition effect enhances by -5.2 kcal/mole the value of the potential minimum near the end water oxygen, thereby accounting for about one-third of the global increase [3]. In the present case, the corresponding addition effect at the locus of the strongest minimum of formamide is -4.8 kcal/mole, also one third of the total enhancement. It may be remarked that the superposition effect most likely represents in reality a larger proportion of the global effect of hydrogen bonding, because the weight of the charge-transfer effect is appreciably exaggerated by the STO 3G basis set.

The situation around the atoms internal to the chain in the dimer is different from that of the end atoms: near the inner oxygen one of the potential minima has been suppressed by H-bonding and one minimum remains, but decreased in value. As observed in other cases, this effect is mainly due, in the region considered, to the strongly positive potential brought about by the proton donor. In the angular dimer of Fig. 1 this effect leaves one decreased minimum close to the oxygen; in a linear dimer with CO \cdots HN aligned (not shown), it leaves two zones of (smaller) negative character on each side of the hydrogen bond (as observed in the linear water dimer [3]). The positive potential of the inner NH region is smaller than that of the end NH₂ group.

When the proton acceptor molecule of the *trans*-dimer is turned 180° about the hydrogen bond axis, the global potential around the end oxygen atom is very little modified except for some symmetrization.

The molecular potential of the cyclic dimer (which involves the binding of NH_c to the O_e side of the carbonyl group in a double manner) presents one negative zone around each oxygen with a minimum nearly equal to the minimum minimum of isolated formamide; in fact the whole map in the OCH region is practically the same as in formamide itself.

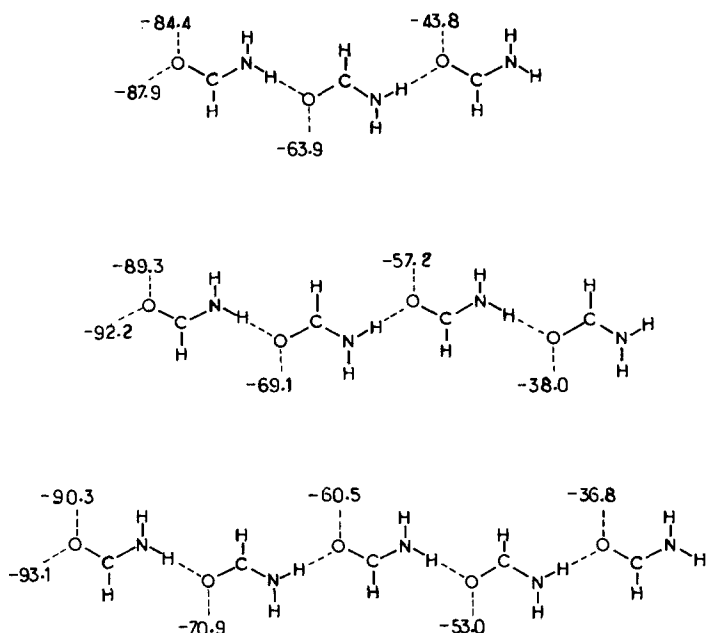


Fig. 2. Values of the minima of molecular potentials near the oxygens in the linear *trans* trimer, tetramer and pentamer

2.2. The Chains of Oligomers

The potential maps in the various regions of the longer *trans*-oligomers have been considered in the same fashion¹. Fig. 2 summarizes schematically the situation at the minima. Fig. 3 gives the values of the potentials computed at a fixed distance (1.715 Å) of each oxygen atom in the directions of the minima, and of each hydrogen of the NH bonds in the bond direction.

The comparison of Figs. 2 and 1 shows that the general character of the end and of inner oxygens is conserved upon elongation of the chain; the enhancement of the end negative potential observed in passing from the monomer to the dimer is further increased in the higher oligomers, although to a lesser and lesser extent, the pentamer end minima being very similar to those of the tetramer. The second largest minimum in every chain is near the oxygen closest to the oxygen end, the next one being the following oxygen. The chains of *trans*-oligomers are thus endowed with a set of negative potential regions near each oxygen atom, the more negative surrounding the end oxygen, with successive minima of decreasing values located along the chain. A similar situation starts at the other end of the chain for the positive potentials: (see the values of Fig. 3) larger values near the two extreme NH protons (with a more positive potential for H *trans* than for H *cis*), and decreasing positive potentials for the successive inner NH bonds along the chain. Note the alternance of positive and negative regions along a chain.

¹ These maps are available upon request.

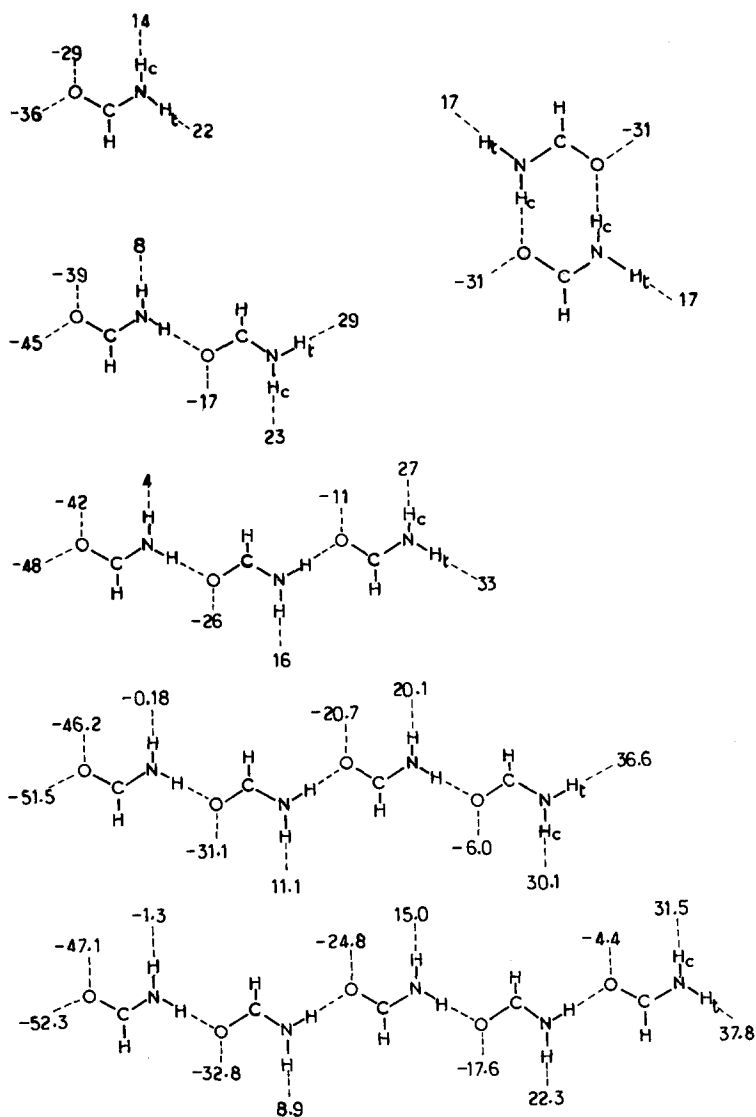


Fig. 3. Values of the potentials at a fixed distance (1.715 Å) of the oxygen atoms in the directions of the minima, and of the hydrogen atoms of the NH bonds along their direction

The very definition of the electrostatic molecular potential [2] as the attraction exerted by a molecule on a point unit positive charge implies that this quantity may serve as a guide in the search of the most probable regions of approach of the proton-donor end of another molecule, and similarly that the regions of positive potential correspond at first approximation to the most attractive regions of approach of an electron-donor atom. This has indeed proved very useful in the preliminary scanning of the possible regions of hydration of various molecules [11–13]. A quantitative utilization of these concepts was recently suggested [14]

for the prediction of hydrogen bond strength, assuming a proportionality of the binding energy to the product $V_D V_A$ of the potentials of the proton-donor D and proton acceptor A taken at a fixed distance of A and D. The potentials given in Fig. 3 can be used in this connection: considering the monomer, the products of the potential values suggest that the best linear dimer should form when the *trans* NH proton of a second monomer binds to the O_i side of the carbonyl oxygen rather than to the O_e side. This is indeed the situation displayed in the computed binding energies [3]: -8.3 against -7.4 kcal/mole respectively (or -8.2 against -7.2 kcal/mole for the corresponding dimers with a 180° rotation around the hydrogen-bond axis). The potentials would predict $O_i H_t$ to be intrinsically more favorable than $O_i H_c$ and $O_e H_t$ more favorable than $O_e H_c$; in the last case however, an appropriate orientation of the second monomer permits the formation of a second $O_e H_c$ hydrogen bond and the energy of each bond is enhanced by the polarization + charge transfer effect of the other as shown by the strong energy (-9.9 kcal/mole per bond) found for the cyclic dimer.

Once the cyclic dimer is formed, the potentials of Fig. 3 would indicate that it is more advantageous to attach on it two monomers through their NH_t proton to the two oxygens of the dimer: product = $(31 \times 22)^2$, than by binding their best oxygen side to the free NH of the dimer: $(36 \times 17)^2$, and that the binding of one monomer by its best oxygen side and that of the other by its NH_t to the two ends of the same molecule in the dimer would be intermediate ($36 \times 17 + 31 \times 22$). The energy of the first complex is not available, but the two others (1 *trans*-tetramer and 1 *cis*-tetramer of Refs. [6] and [7]) are indeed in the order predicted (-8.7 and -9.4 kcal/mole per H bond respectively [7]). The potentials also predict that the hydrogen bond between two *trans* linear dimers established so as to form the all-*trans* linear tetramer ($V_A V_D = 29 \times 45$) should be more favorable than that between two cyclic dimers arranged so as to form a bicyclic compound ($V_A V_D = 31 \times 17$). Indeed the corresponding energies computed from the data of Refs. [6] and [7] are -12.6 and -7.2 kcal/mole. Similarly the bonding together of two *trans*-linear dimers will proceed using the end O_i of one and the end NH_t of the other rather than its NH_c (energies 8.7 and 7.1 kcal per H bond respectively [4-5]). It is obvious, in spite of these favorable examples that the correlation must be used with caution as soon as the contacts between the entities in interaction become complex. With this reservation in mind, the potentials of Fig. 3 seem to indicate that once the *trans* linear dimer is formed the further addition of a monomer by one hydrogen bond will rather proceed by sequential H bonding at its ends (preferably by using O_i and NH_t) than by branching in the middle, this process continuing in the successive oligomers, seemingly favouring the formation of all *trans* chains. The formation of a cyclic dimer on a linear dimer does not seem very favourable according to the potential values but such a formation on the central molecule of a trimer cannot be excluded. The choice between prior elongation of a chain longer than a dimer and prior local formation of cyclic dimers on it is not possible on this basis.

Finally an interesting remark may be made considering the distribution of the potentials in the chains: should two or more chains be packed together, they

would tend to lie antiparallel to one another so that the most negative potentials at the end of one chain face the most positive ones at the end of the other, the arrangement being further favoured by the fact that the negative potentials of the inner oxygens of one chain face the positive potentials of the inner free NH groups of the other and conversely, thus favouring the formation of successive cyclic dimers between the chains. This structure is indeed the arrangement observed in the crystal [15] in the successive sheets.

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References

1. The role of the electrostatic potential in chemistry. Symposium of the American Chemical Society, Houston, Texas, April 1980
2. Bonaccorsi, R., Scrocco, E., Tomasi, J.: *J. Chem. Phys.* **52**, 5270 (1970)
3. Pullman, A., Berthod, H.: *Theoret. Chim. Acta (Berl.)* **48**, 269 (1978)
4. Dreyfus, M., Maigret, B., Pullman, A.: *Theoret. Chim. Acta (Berl.)* **17**, 109 (1970)
5. Dreyfus, M., Pullman, A.: *Theoret. Chim. Acta (Berl.)* **19**, 20 (1970)
6. Hinton, J. F., Harpool, R. D.: *J. Am. Chem. Soc.* **99**, 349 (1977)
7. Pullman, A., Berthod, H., Giessner-Prettre, C., Hinton, J. F., Harpool, D.: *J. Am. Chem. Soc.* **100**, 3991 (1978)
8. Hehre, W. J., Stewart, R. F., Pople, J. A.: *J. Chem. Phys.* **51**, 2657 (1969)
9. Berthod, H., Pullman, A.: *Chem. Phys. Letters* **14**, 217 (1972)
10. Bonaccorsi, R., Pullman, A., Scrocco, E., Tomasi, J.: *Chem. Phys. Letters* **12**, 622 (1972)
11. Pullman, A., Armbruster, A.-M.: *Chem. Phys. Letters* **36**, 558 (1975)
12. Pullman, A., Berthod, H., Gresh, N.: *Chem. Phys. Letters* **33**, 11 (1975)
13. Orita, Y., Pullman, A.: *Theoret. Chim. Acta (Berl.)* **45**, 257 (1977)
14. Kollman, P. A.: *J. Am. Chem. Soc.* **99**, 4875 (1977)
15. Ladell, J., Post, B.: *Acta Cryst.* **7**, 559 (1954)

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