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Relationes

On the Molecular Electrostatic Potentials Obtained from CNDO Wave Functions

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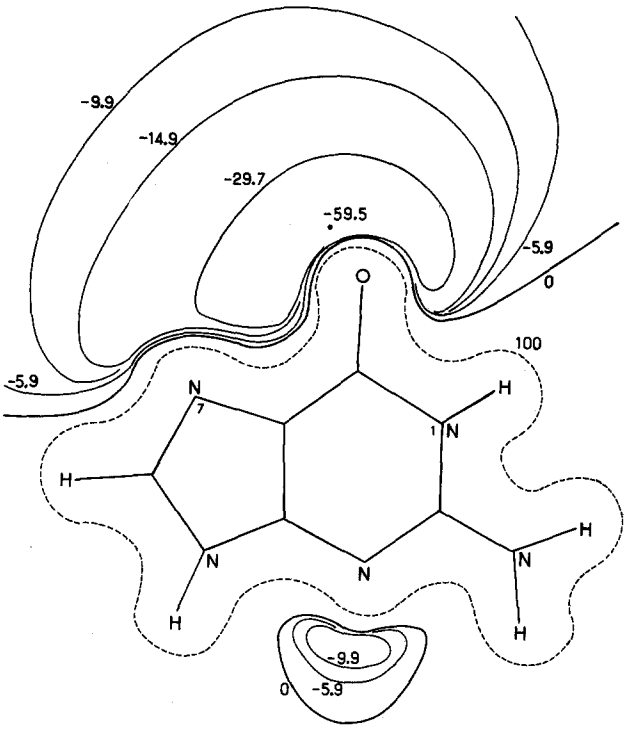
The various approximations proposed for computing molecular potentials with CNDO wave functions are tested on the case of guanine and shown to be unable to reproduce correctly the essential fine features of the *ab initio* potential.

Key word: Guanine

One of the aims of our previous work [1–3] on the calculation of the electrostatic potential created by a molecular charge distribution in the space surrounding the molecule was the development of a reliable approximation which would permit to avoid the "*ab initio*" level in this type of calculation [4–12] and allow the use of wave functions obtained by semi-empirical methods in the case of large molecules. Detailed studies with CNDO wave functions led us to conclude that valuable informations on the gross features of the most attractive regions for electrophilic attack could be obtained in the γ_{ss} or, better, V_{ss} approximations (see Refs. [1–3]) but that an accurate representation required both the deorthogonalization of the wave function and the use of *all* the terms $P_{\mu\nu}V_{\mu\nu}$ in the expression of the electronic part of the potential. Recently we have shown that, even within this technique, an inversion occurs in the order of the in-plane vicinal minima of oxygen and nitrogen in cytosine (with respect to the *ab initio* order) with both CNDO and INDO wave functions [3].

In the present Note we would like to investigate further the problem of the various approximations and their validity. This study was prompted by a recent suggestion [13] that good potential maps could be obtained with CNDO or INDO functions without deorthogonalization, by keeping only the diagonal elements of the density matrix (as in the V_{ss} approximation) but without averaging the nuclear attraction integrals over *s* orbitals. This differs from our approximation III of Ref. [2] by the neglect of the one-center *sp* and *pp'* terms. Only one case however (formaldehyde) served as an illustration of the validity of this approximation. We have presently tested it on a larger and more complex molecule in view of possible applications on a wider scale. We have chosen for this sake the molecule of guanine because its *ab initio* molecular potential has recently become available [14], giving thus a good ground for comparison. Moreover the structure of guanine is complex enough to provide a good example of possible artefacts comparable to those encountered previously [3]. In order to appreciate


-9.9
-14.9
-29.7
-59.5
-5.9
0
100
-5.9
O
N
7
H
1
N
H
H
N
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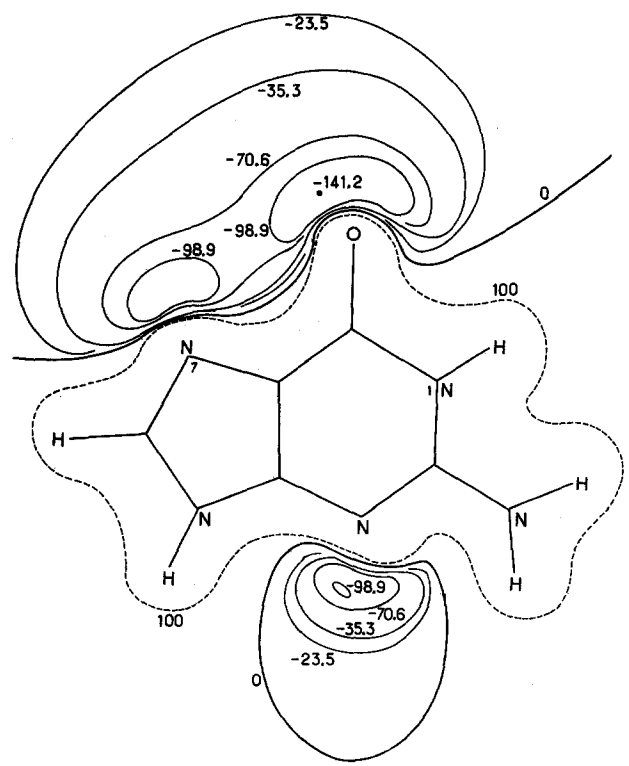
N
H
H
H
-9.9
0
-5.9

(a)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-35.3
-70.6
-141.2
0
-98.9
-98.9
O
100
N
7
H
1
N
H
H
N
N
N
H
H
H
-98.9
-70.6
-35.3
-23.5
100
0

(b)

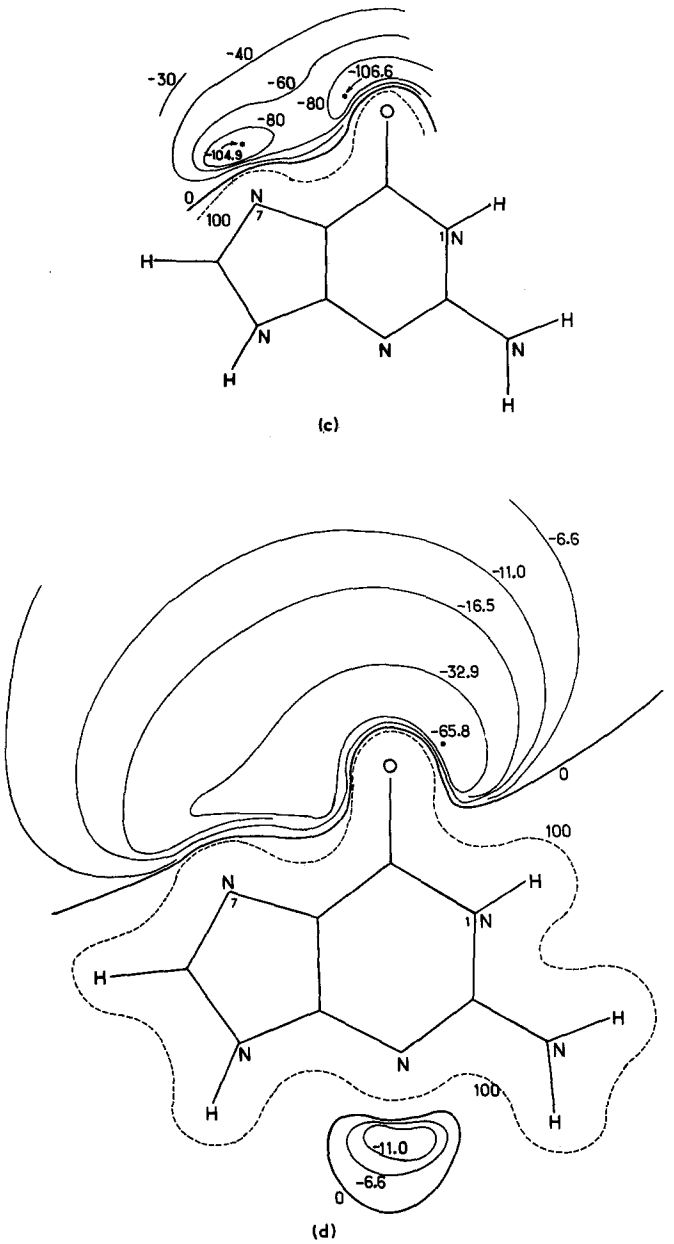

Fig. 1a–d. Isoenergy curves of guanine calculated from the CNDO wave function according to: (a) the V_{ss} approximation, (b) introduction of all two-center integrals, (c) deorthogonalized wave function and all integrals, (d) approximation due to Caballol *et al.* [13]

all the possible levels of computations we have drawn the isopotential maps in the molecular plane (Fig. 1) using our former approximations, II, III and IV of Ref. [2] as well as the new one of Ref. [13]. (Approximation I (γ_{ss}) has been given in [1].) These maps are reproduced in Fig. 1a–d respectively.

It may be seen (Fig. 1a) that the V_{ss}-map is qualitatively identical with the γ_{ss}-one, with a large attractive region encompassing the N_7 and O-atoms but with only one minimum closer to the oxygen atom, in contrast to the *ab initio* results [14] where two minima appear, the deeper one facing the nitrogen atom. The situation is very similar to that encountered in cytosine [3].

Approximation III (Fig. 1b) which distinguishes between the atomic orbitals *s*, *x*, *y*, *z*, and keeps the one-center *sp* and *pp'* terms allows the obtention of two distinct potential wells near N_7 and the oxygen of the carbonyl group as do the non-empirical computations, but it indicates the oxygen as being the most attractive toward H^+ or any electrophilic agent (141.2 kcal/mole for O and 138.6 kcal/mole for N_7) while the *ab initio* wells are respectively of 75 and 91 kcal/mole. In addition we can remark that the potential wells are nearly twice too deep when compared to the non-empirical ones. This confirms our preceeding conclusion [2] based on the computations for water and formaldehyde, that approximation III leads to values of the potential which are numerically too large.

The map of Fig. 1c corresponding to the deorthogonalized approximation function and all integrals has been explored only in the upper region for economy reasons. It is seen that, qualitatively, it is very similar to the previous one. The only difference is the depth of the potential wells in the region of space we are interested in. Numerically, approximation IV gives values which are closer to the *ab initio* ones (106.6 kcal/mole for the carbonyl oxygen and 104.9 for N_7), but the inversion of the order remains, so that even the very elaborate calculation is unable to predict the protonation at N_7, rather than on the oxygen, which is in fact the order observed experimentally (see [14] for a detailed discussion). We have had a similar failure for cytosine: the same type of computations found that the oxygen rather than N_3 should be protonated, in contradiction with *ab initio* results [7] as well as with experiment [15].

If we consider in Fig. 1d the map corresponding to the proposal of Caballol *et al.* [13] we see that it is very similar to the one obtained from the V_{ss} approximation: there is only a single large well surrounding the carbonyl oxygen and extending towards N_7. Moreover although the well is somewhat more extended toward N_7 than in Fig. 1a, the new approximation has an additional major defect in that it predicts the bottom of the well of the carbonyl oxygen to be on the side opposite to N_7 with respect to the CO bond. All the previous approximations agree with the non-empirical results to locate this well on the same side of the CO bond as N_7. In addition the numerical agreement with *ab initio* results for the depth of the well is not good in the present case.

In conclusion, the comparison of the electrostatic potential maps of guanine presented here with the corresponding non-empirical results shows that it is necessary to introduce at least all the density matrix elements and the corresponding integrals between atomic orbitals located on a same center, in order to predict two distinct attractive wells for a pyridine-like nitrogen vicinal to a carbonyl oxygen. The results are somewhat numerically improved if the wave

function is deorthogonalized and the three center integrals introduced. However none of the calculations is able to reproduce the preference for N_7 over the oxygen obtained unequivocally in the *ab initio* results. This defect confirms the exaggeration already observed [3, 16] of the oxygen attractive potential with respect to that of nitrogen when CNDO wave functions are utilized. These functions should thus be used with extreme caution in the search of molecular potentials.

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