

Molecular Electrostatic Potential Surfaces of 3-Methoxy-2-Propenone. A Comparison Between CNDO/2 and *Ab Initio* Calculations

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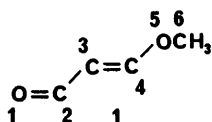
Molecular electrostatic potential surfaces of *trans*-3-methoxy-2-propenone have been calculated using semi-empirical CNDO/2 molecular orbital calculations and *ab initio* molecular orbital calculations at the STO-3G and 4-31G levels.

Knowledge of the molecular electrostatic potential (MEP) around a molecule is very important in applications such as computer-aided molecular design and for understanding the reactivity of a compound.¹⁻⁵

The MEP at a point P , $V(P)$ is calculated using eqn. 1, where the first summation is made over the nuclei of the molecule and the second is made over all the electrons.

$$V(P) = \sum_A \frac{Z_A}{R_{PA}} - \sum_{\mu\nu} P_{\mu\nu} \int \frac{\chi_\mu \chi_\nu}{r} d\tau \quad (1)$$

Consequently, the theoretical problem is not so much one of calculating the MEP, but rather of which level of approximation to use. There is probably no general solution to this latter problem. One must clearly define what the MEP is to be used for and choose the level of approximation accordingly. This is easily said, but how does one do this? The purpose of this paper is to provide one example of MEP surfaces calculated at various levels of approximation. *trans*-3-Methoxy-2-propenone (TMP), **1**, was chosen as the model compound because it contains a planar unsaturated part, an ether oxygen with lone-pair electrons and an alkyl group.



At an appropriate distance above the molecular plane defined by the unsaturated part, the MEP surface for this compound should be able to detect the influence of the sp^2 -hybridized atoms, the lone-pairs on the ether oxygen and the steep gradient of the MEP caused by the nearby methyl group.

How does the input structure affect the MEP? Common practice is to use a structure obtained by X-ray analysis, a standard geometry or a structure optimized by some other molecular mechanics or quantum mechanical method. If the MEP of a compound is not calculated using the same method by which the structure of the compound was previously optimized then an error is introduced, since the structure is no longer energy-minimized from the MEP methods point of view. Does this error affect the MEP to any significant extent? In order to try to shed some light on this question the MEP of TMP has been calculated using *ab initio* methods at the STO-3G and 4-31G levels of approximation, both with optimized geometries and with geometries obtained from molecular mechanics calculations.

Methods of calculation

The semi-empirical CNDO/2 molecular electrostatic potential (MEP) surfaces⁶ were calculated using a geometry obtained from molecular mechanics calculations (MM2PI). MM2PI is a com-

bination of the VESCF part of MMPI and the potential functions of MM2. MM2PI is similar to the MMPI-MM2 hybrid method presented by Lipkowitz *et al.*⁷ For a description of MMPI and MM2, see Ref. 8. The *ab initio* MEP surfaces were calculated by the GAUSSIAN 80 program (UCSF version)⁹ at the STO-3G and 4-31G levels using the geometry described for CNDO/2. *Ab initio* MEP surfaces with complete geometry optimization at the STO-3G and 4-31G levels were also calculated. The computations were performed either on a VAX 11/785 or on a VAX 8600.

The MEP maps of TMP were calculated 1.6 Å and 3.0 Å above the plane defined by the unsaturated part of the molecule.

Results and discussion

CNDO/2 calculations. The MEP of **1** calculated by the CNDO/2 method (Figs. 1 and 2) were too positive compared with the ones predicted by *ab initio* calculations. The use of the CNDO/2 approximation, in which the nuclear attraction integrals are approximated by minus the repulsion integrals between *s* orbitals, leads to this result. This is a fact also observed by other authors.¹⁰⁻¹¹ However, the positions of the global minimum near the carbonyl moiety and of the maximum

Table 1. Geometries of *trans*-3-methoxy-2-propenone. Bond lengths in Å and angles in degrees.

Atoms	MM	STO-3G	4-31G
1-2	1.2174	1.2213	1.2141
2-3	1.4739	1.4999	1.4500
3-4	1.3509	1.3206	1.3221
4-5	1.3534	1.3915	1.3490
5-6	1.4208	1.4369	1.4346
1-2-3	125.11	124.46	124.86
2-3-4	121.72	121.56	119.48
3-4-5	123.43	121.39	122.84
4-5-6	115.80	112.33	119.42
1-2-3-4	-179.88	-179.83	-179.48
2-3-4-5	-179.66	-179.42	-179.85
3-4-5-6	-173.54	-173.81	-174.22

near the methyl group are predicted correctly. What is more serious is the fact that the influence of the lone-pairs of the ether oxygen as well as that of the *sp*²-hybridized system of TMP is largely neglected. In fact, CNDO/2 predicts a potential maximum over the double bond (Fig. 1).

One must, therefore, be very careful when using MEP surfaces based on CNDO/2 since they provide, at best, only qualitatively correct maps. It is recommended to check the CNDO/2 results by *ab initio*-based calculations to see how well the former MEP agree with the latter in each particular case. If the agreement is reasonable then the

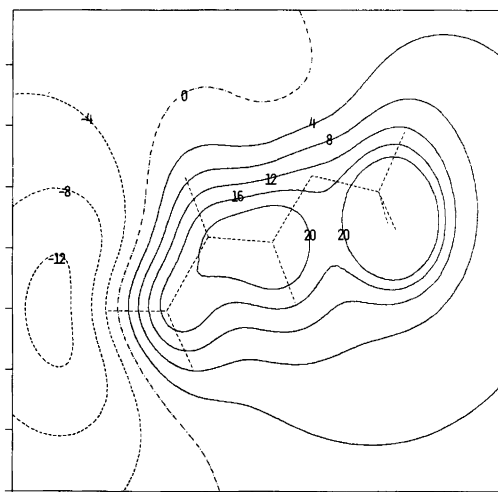


Fig. 1. CNDO/2 MEP surface at 1.6 Å.

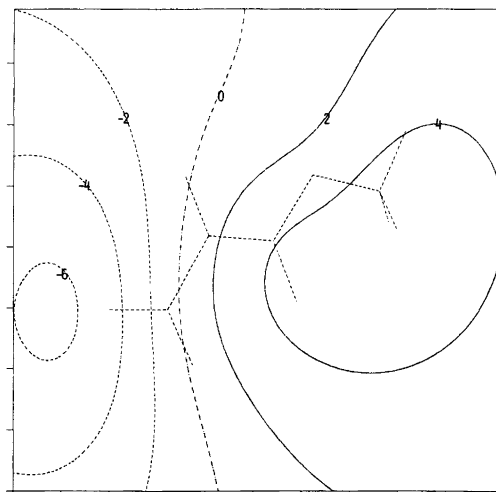


Fig. 2. CNDO/2 MEP surface at 3.0 Å.

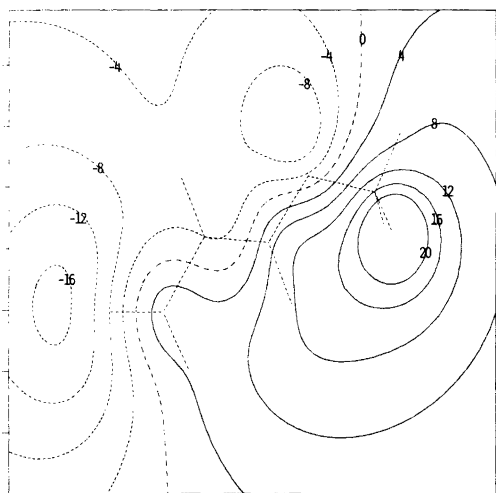


Fig. 3. *Ab Initio* (STO-3G) MEP surface at 1.6 Å.

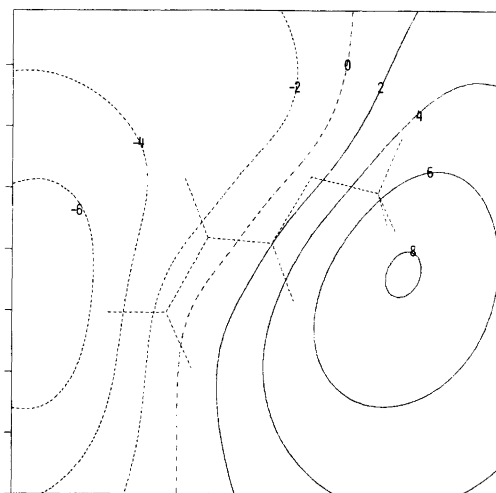


Fig. 4. *Ab Initio* (STO-3G) MEP surface at 3.0 Å.

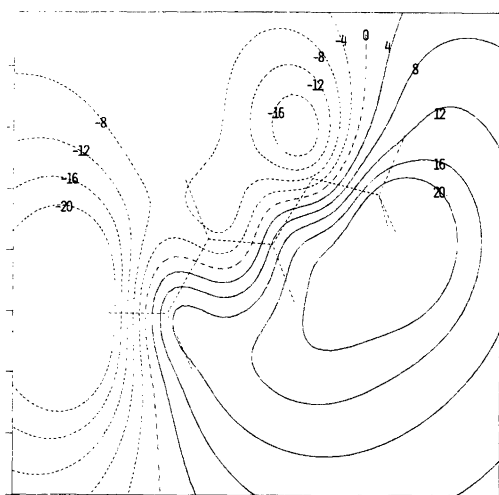


Fig. 5. *Ab Initio* (4-31G) MEP surface at 1.6 Å.

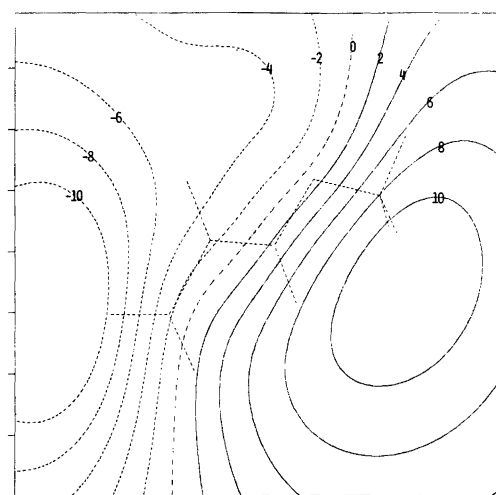


Fig. 6. *Ab Initio* (4-31G) MEP surface at 3.0 Å.

CNDO/2 method can be used to quickly examine interesting related compounds to obtain a first approximation for the MEP surfaces of these latter compounds. *Ab initio* calculations can then be made for selected structures of interest.

Ab initio calculations. *Ab initio* calculations based on the molecular mechanics geometry of TMP, using two basis sets (STO-3G, Figs. 3 and

4; 4-31G, Figs. 5 and 6), both predict the same characteristics for the MEP surfaces. Thus, the calculations place the global minimum and the global maximum close to the carbonyl oxygen and the methyl group, respectively, as well as recognizing the local minimum due to the orientation of the lone-pairs of the ether oxygen and the influence of the carbon-carbon double bond. However, there are slight differences between

Table 2. Maxima and minima on the molecular electrostatic potential surfaces of *trans*-3-methoxy-2-propenone.

Distance ^a	1.6 Å		3.0 Å	
	Min. ^b	Max.	Min.	Max.
Sto-3G//MM ^c	-16.90	31.17	-7.43	8.12
4-31G//MM	-32.84	40.36	-13.30	11.83
STO-3G//STO-3G	-15.36	27.16	-6.62	7.28
4-31G//4-31G	-33.73	36.86	-13.64	11.82
CNDO/2//MM	-13.22	49.98	-6.34	5.28

^aDistance above the molecular plane defined by the unsaturated part of TMP. ^bIn kcal mol⁻¹. ^cSTO-3G//MM means that the STO-3G basis set was used to calculate the MEP with a geometry optimized by molecular mechanics.

the MEP surfaces when using the minimum basis set (STO-3G) and the extended (split valence) basis set (4-31G). STO-3G predicts a flatter surface than 4-31G (Table 2). It also places the global minimum at a slightly larger distance from the carbonyl oxygen (1.09 *contra* 0.82 Å). MEP surfaces obtained at 3-21G and 6-31G levels of approximation are virtually identical with those at the 4-31G level.¹²

MEP surfaces calculated using geometries optimized at the same level of calculation do not change the geometries to any significant extent. The most marked effect is at the STO-3G level of approximation, where the MEP surfaces become even flatter using a STO-3G optimized geometry than those based upon a molecular mechanics geometry. This is not a very surprising result since it is well known that the minimum STO-3G basis set does not predict good geometries. It is, therefore, advisable to use the STO-3G basis set to calculate MEP surfaces only when using a good input geometry obtained by some other method. The MEP surfaces of TMP calculated using the 4-31G basis set with a 4-31G optimized geometry are virtually identical with the ones obtained at the same level of approximation using a molecular mechanics geometry. The small differences that exist are negligible for most purposes.

Conclusions

The MEP of TMP calculated using CNDO/2 molecular orbital calculations show that the method must be used with great care and that it gives only qualitatively correct results. The *ab initio* molecular orbital calculations using various basis sets

predict very similar MEP of TMP. A reasonable level of approximation seems to be that employing the STO-3G basis set with an input geometry obtained by some other method.

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