# Benzamidoximes: Configuration, Conformation, and Reactivity. Molecular Orbital Calculations

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MO-SCF-FORCE calculations on benzamidoxime confirm the amino-oxime tautomer as being the more stable and explain the anomalous chemical behaviour of the $NH_2$ function.

Our interest in benzamidoximes has been stimulated as a result of our work with phenyloxadiazolines, for which benzamidoximes serve as starting material. Evidence favouring the amino-oxime (I) tautomer (Figure 1) over α-hydroxyaminobenzylideneamine (II) (Figure 2) at room temperature in both solution and solid phases has been presented [1] based on i.r. and n.m.r. results. Previously, the former tautomer had been assumed to be the more stable and the configuration of this form was

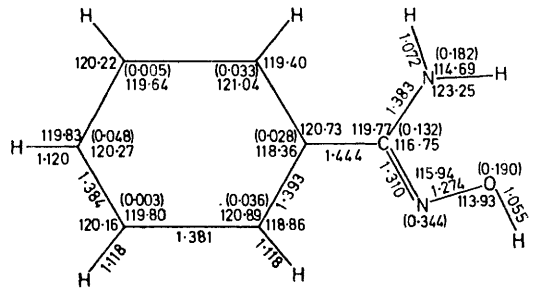


Figure 1 Bond angles (°) and lengths (Å) obtained by the FORCE method for the most stable configuration of the amine–oxime conformation (I) of benzamidoxime. Non-zero HOMO electron densities (atomic) are shown in parentheses

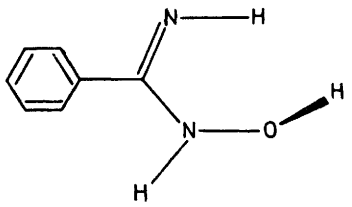

Figure 2 Calculated most stable configuration of the α-hydroxyaminobenzylideneamine conformation (II) of benzamidoxime

found [2] to be *syn-Z* (see Figure 1) on the basis of electric dipole moment data. These conclusions have been confirmed [3] more recently on the basis of electric dipole moment and n.m.r. results.

Acylation of amidoximes under neutral conditions results [4,5] in *O*-acylation and not the expected *N*-acylation, except in the case [4] of formamidoxime where both acylations occur. In an earlier report,[6] one of the acylation reactions was found to afford both *O*- and *N*-acylation products of formamidoxime. Recently, an effort [7] in our laboratory to condense *O*-methylbenzamidoxime with propionaldehyde to form *O*-methyl-*N*-propylidenebenzamidoxime was also unsuccessful. Thus, it is clear that the $NH_2$ group in benzamidoxime (and most other amidoximes) does not behave like a normal amine function.

Extended Hückel calculations have been reported [8] for various configurations and conformations of *N*-methylbenzamidoxime, and the calculated energies compared. To our knowledge, there is no reported work dealing with molecular orbital calculations on benzamidoxime itself, nor has an explanation been given of its anomalous chemical behaviour for the acylation reaction.

We report here the results of CNDO/2-FORCE calculations on various configurations of the two possible tautomers of benzamidoxime and formamidoxime. The results for the calculated lowest energy form are compared to the known physical properties of the ground state and chemical reactivity is explained by comparing results for the two molecules.

## METHODS

All calculations were done on the Burroughs B 6700 computer at the Núcleo de Computação Eletronica of the Universidade Federal do Rio de Janeiro. The method was basically CNDO/2 (the self-consistent field criteria have been given [9] previously) starting with standard geometries [10] and minimizing the energy with respect to the co-ordinates until not a single force element [11] was greater than 0.1 mdyn.

## RESULTS

The Table shows the calculated energies, dipole moments, and HOMO electron densities, charges, and electrophilic superdelocalizabilities [12] of the oxygen and amino nitrogen atoms for the most stable configuration of each tautomeric form of both benzamidoxime and formamidoxime. Bond distances, bond angles, and HOMO electron densities (in parentheses) on all atoms are given in Figure 1 for the stablest form of benzamidoxime only.

## DISCUSSION

In addition to the calculated most stable configuration agreeing with previously cited [2-4] results for benzamidoxime, we find the same relative stability for formamidoxime which has been reported [13] on the basis of *X*-ray results. In the case of benzamidoxime, all reasonable geometries for tautomer (I) are planar. Any attempt to take the hydrogens of the $NH_2$ group or the OH group out of the plane of the molecule gave ground state energies which were higher than the planar forms by 2 eV or more. Even a slight deviation of the amino oxime

Calculated energies, dipole moments, and reactivity indices of the tautomeric forms of formamidoxime and benzamidoxime

| Compound | Tautomer | $E_{rel}$/ kcal mol$^{-1}$ | $\mu$/D | HOMO N | HOMO O | Charge $q_N$ | Charge $q_O$ | S.e.[a] N | S.e.[a] O |
|---|---|---|---|---|---|---|---|---|---|
| Formamidoxime | (I) | (0) | 1.55 | 0.316 | 0.206 | −0.220 | −0.167 | −0.130 | −0.146 |
| | (II) | 18.3 | 3.92 | 0.332 | 0.063 | −0.258 | −0.133 | −0.143 | −0.137 |
| | Experimental | (I) < (II) | 2.26 [b] | | | *O*- and *N*-acyl derivatives | | | |
| Benzamidoxime | (I) | (0) | 1.51 | 0.182 | 0.190 | −0.242 | −0.162 | −0.133 | −0.147 |
| | (II) | 20.1 | 3.86 | 0.408 | 0.039 | −0.280 | −0.133 | −0.149 | −0.138 |
| | Experimental | (I) < (II) | 1.78 [c] | | | *O*-acyl derivative | | | |

[a] Electrophilic superdelocalizabilities. [b] R. Raman and S. Soundararajan, *Proc. Indian Acad. Sci.*, 1958, **47A**, 357. [c] J. Barassin, J. Armand, and H. Lumbroso, *Bull. Soc. chim. France*, 1969, 3409.

group from the plane of the phenyl ring caused a considerable increase in energy. Form (II) was calculated to be most stable in a non-planar configuration (see Figure 2). Between the two tautomers (I) and (II) all planar configurations of (I) are calculated to be more stable than all configurations of (II) by *ca.* 1 eV. The dipole moments calculated agree reasonably well with experiment, and leave little doubt regarding which configuration is present.

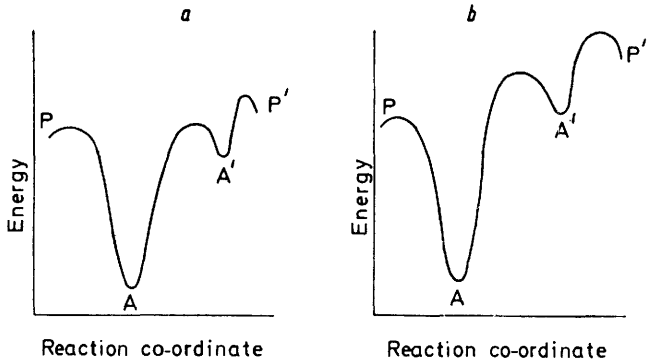


FIGURE 3 *a*, Tautomeric form (A′) of reagent (A) has an activation energy comparable with that of the direct reaction to product (P) thus allowing the formation of the product (P′) of the tautomeric form. *b*, Direct product is attained more easily than tautomeric form, favouring production of P

We explain the anomalous, exclusive *O*-acylation of benzamidoxime as compared with the *O*- and *N*-acylation of formamidoxime on the basis of the following argument. Chemical reactivity is determined by the properties of the activated complex along the reaction path and not necessarily by the most stable ground-state configuration,[14] as is often assumed. (Unfortunately, the FORCE method is not very useful in determining the structure and energy of the activated complex for large molecules, because it automatically searches out an energy minimum, whereas the complex is located at a saddle point.) One can visualize two possible cases. In Figure 3*a* the transition state for A ⟶ A′ is of comparable energy with the transition state for the process A ⟶ P. Figure 3*b* represents the case where the A ⟶ A′ transition state is of higher energy than the A ⟶ P transition state. Hence A ⟶ P is heavily favoured over A ⟶ P′ in cases where Figure 3*b* describes the energetics of the system; however, P′ could be the predominant product under irreversible conditions in cases such as Figure 3*a*.

It is suggested that formamidoxime is *O*- and *N*-acylated *via* both tautomeric forms following the reaction scheme represented in Figure 3a, while benzamidoxime is *O*-acylated *via* the amino-oxime form as in Figure 3*b*. One notes for both molecules that all three reactivity indices (Table) show that the tautomeric form (II) is more subject to *N*-acylation than the stabler form (I). This inversion in preference is best shown by the electrophilic superdelocalizabilities. One can arrive at a similar conclusion on the basis of valence bond theory by drawing resonance structures for possible intermediates in tautomers (I) and (II) after electrophilic attack of a carbonyl carbon on either the oxygen or nitrogen. One notes that of the four possibilities, the only reasonable structure which is expected to be stabilized by charge delocalization is the *N*-acylated tautomeric form (II).

A possible justification for formamidoxime attaining the alternative tautomeric form more easily than benzamidoxime can be found in considering solvation energies in commonly used polar acylation media. In general, the imine form (II) will be stabilized by solvation more than the amino-oxime form (I), because of the higher dipole moments of the former. In the Kirkwood approximation,[15] the solvation energy (neglecting PV and TS terms) is given by $E \propto r^{-3}$ where $r$ is the ' effective radius ' of the solute. Hence, the solvation stabilization for formamidoxime in form (II) will be greater than for benzamidoxime in form (II), because of the latter's greater size. A rough calculation, using the Kirkwood formula,[15] indicates an additional 2—3 kcal mol$^{-1}$ solvation energy gain for form (II) in formamidoxime compared with benzamidoxime. This, added to the 1.8 kcal mol$^{-1}$ (Table) calculated for the isolated molecules, makes the argument at least plausible, in our opinion, if not absolutely convincing.

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