



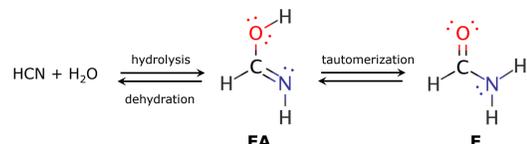
Natural Bond Orbital Analysis of Formimidic Acid Reactions

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Introduction

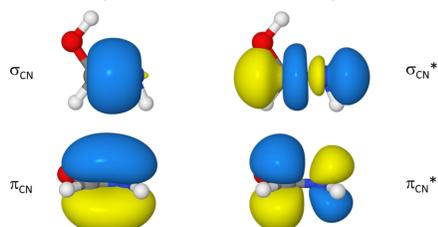
Hydrogen cyanide (HCN) and formamide (F, $\text{NH}_2\text{CH}=\text{O}$) are two small molecules observed in interstellar media. The latter can be produced from the former by hydrolysis via a formimidic acid (FA, $\text{HN}=\text{CHOH}$) intermediate.



FA has been studied in cryogenic matrices [1,2] and by computational chemistry methods [3,4]. It is about 12 kcal/mol less stable than F.

In this study we use computational chemistry calculations (B3LYP with the 6-311++G** basis set) and natural bond orbital (NBO) analysis [5] to address aspects of FA chemistry. NBO analysis is a popular method for expressing the character of complex electron densities in terms of localized orbital concepts (e.g. hybridization, bonds, lone pairs, Lewis structures, resonance). These concepts form the common framework of the bench chemist's understanding of chemical structure and reactivity.

Antibonds are key actors in NBO analysis. Every bond (the in-phase combination of a pair of atomic hybrids) has a corresponding antibond (the out-of-phase combination). The following are examples of bond/antibond pairs in FA.

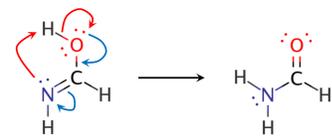


Although formally empty—and therefore often neglected—antibonds act as electron acceptors, allowing electrons to delocalize in molecules and facilitating electron redistribution during chemical reactions. Consider, for example, NBO analysis of FA [6] at its equilibrium geometry:

#	Structure	Weight (%)	Donor-Acceptor Interaction
FA1		64.2	
FA2		20.2	$n_{\text{O}} \rightarrow \pi_{\text{CN}}^*$ (40.4)
FA3		10.1	$n_{\text{N}} \rightarrow \sigma_{\text{CH}}^*$ (10.7)
FA4		3.7	$\sigma_{\text{NH}} \rightarrow \sigma_{\text{CO}}^*$ (10.6)

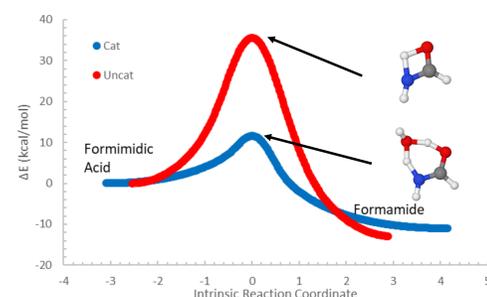
Tautomerization

FA and F interconvert via tautomerization, a simple 1,3-proton transfer between O to N. The organic chemist depicts this reaction using the electron pushing mnemonic ("curved arrows") as follows:

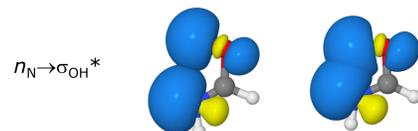


Red arrows show the formation of the new N-H bond and cleaving of O-H, and blue arrows show the redistribution of π electrons that effectively shift the double bond to form the carbonyl (C=O) of F.

We calculated the intrinsic reaction coordinate—the energy profile—for tautomerization. This is shown in the following figure in red, as FA (on the left) passes through the transition state (with a 35 kcal/mol barrier) to form F (on the right).

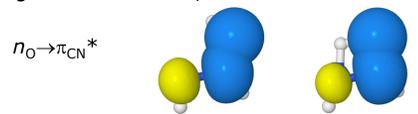


Donor-acceptor orbital interactions facilitate the reaction. Below is the interaction between the "filled" N lone pair and the "empty" OH antibond in the reactant geometry (on the left) and at the transition state (on the right).



Weak orbital overlap in the reactant inhibits the transfer of electron density ($\sim 0.005e$) from the lone pair into the antibond. In contrast, at the transition state, strong overlap allows considerable electron density ($\sim 0.260e$) to move from the lone pair into the antibond. Electron transfer acts to form the new N-H bond and break the O-H bond, the same rearrangement shown above with red arrows.

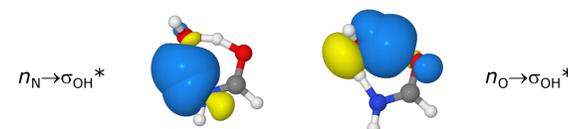
Meanwhile, electron density in an out-of-plane O lone pair delocalizes into the C-N π^* antibond. Below is a view of this orbital overlap from above (looking down on the π system). Electron transfer yields C=O double bond character while cleaving the C=N π bond, consistent with blue arrows above.



Catalyzed Tautomerization

Intramolecular tautomerization has a rather high activation barrier (~ 35 kcal/mol relative to FA) and will not readily occur. A solvent molecule, such as H_2O , can catalyze the rearrangement via intermolecular proton transfer. A single water molecule yields a six-membered cyclic transition state that reduces the barrier to about 12 kcal/mol (as shown on the left in blue).

Two donor-acceptor interactions stabilize the transition state for intermolecular tautomerization.



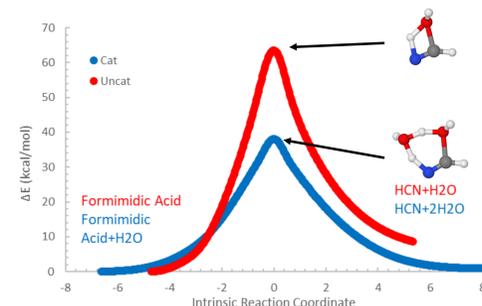
These orbitals are better aligned and more strongly overlapping in this transition state than in the uncatalyzed transition state, thereby reducing the reaction barrier.

Dehydration

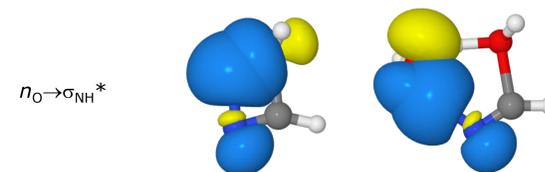
We also examined the dehydration of FA to produce HCN.



The uncatalyzed reaction has a barrier of nearly 75 kcal/mol (below in red). Adding a single water molecule reduces the barrier to about 38 kcal/mol (in blue).



Intramolecular (uncatalyzed) and intermolecular (catalyzed) interactions of an O lone pair with the N-H antibond facilitate the reaction. These interactions cleave the N-H bond and form a new O-H bond as a proton transfers to O, consistent with the red curved arrows shown above. More favorable overlap in the catalyzed reaction stabilizes the transition state and yields a lower reaction barrier.



Promoting NBO Usage

NBO program development is a 25-year collaborative effort between the University of Wisconsin-Madison and Indiana State University. NBO7 [5] was released in November 2018. As of June 2021, 569 individual or site licenses (identified below) have been distributed to users worldwide,



and NBO7 has already been cited in the literature over 1500 times. The present project stems from a contribution to a forthcoming text on computational chemistry methods that will provide instruction to new NBO users.

Conclusions

Donor-acceptor orbital interactions facilitate redistribution of electron density in chemical reactions. Favorable orbital overlap leads to bond formation while electron transfer into antibonding orbitals acts to cleave bonds. Energy barriers for tautomerization and dehydration of formimidic acid decrease when a solvent molecule catalyzes proton transfer. The reduced barriers stem from stronger orbital interactions in the catalyzed reactions. NBO analysis provides users a detailed and intuitive description of the nature of chemical structure and reactivity.

Acknowledgements

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