

Resonance Interactions in Acyclic Systems. 4. Stereochemistry, Energetics, and Electron Distributions in 3-Center Four- π -Electron Systems A=B-C:

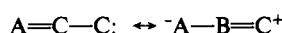
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Abstract: The origin of the larger formation constants for oximes as compared to imines has been examined theoretically. The structures of the conformers of *N*-fluoroacetaldimine (1), acetaldoxime (2), acetaldehyde hydrazone (3), and *N*-methylacetaldimine (4) have been calculated using the 6-31G* basis set. The formation energies determined at the 6-31+G* level, including correction for zero-point energy differences, increased in the order 4, 3, 2, 1. The larger formation constant for 1 as compared to 3, despite the lower energy of the lone-pair electrons on F as compared to N, shows that resonance stabilization is not the factor that controls the thermochemistry of the processes. The bond and atom properties of the compounds have been investigated, and it was found that the sum of the electron populations on N and its substituent, X, was essentially constant and that the effect of X was to control the ratio of the populations at the two groups. The more stable 1 had an essentially equal charge distribution between N and X. The origins of the differences in formation constants were analyzed with the use of isodesmic reactions, and they appeared to result from differences in lone-pair repulsion between the N and X atoms in the amine reactant and imine product. The question of when π -electron delocalization leads to energetic stabilization is discussed.

1. Introduction

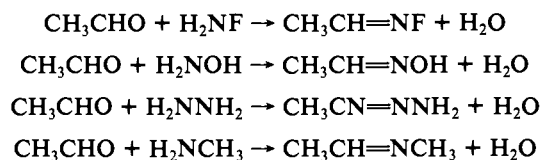
Resonance interactions have played an important role in the development of a theoretical understanding of organic chemistry.¹ Phenomena in acyclic systems that have been explained using such interactions include the greater acidity of carboxylic acids as compared to alcohols,² the barriers to rotation in amides and esters,³ the larger formation constants for oxime formation than for imine formation,⁴ and the lower acidity of esters as compared to ketones.⁵ These interactions appear to be very commonly invoked in systems such as the following:



One might, however, have some reservations about the contribution of the dipolar structure. Perturbation theory indicates that the magnitude of the interaction between the canonical structures is inversely proportional to the difference in energy between them.⁶ In the above case, one might reasonably expect that the dipolar structure should have a significantly higher energy than the normal structure and therefore would not contribute much to the structure of the resonance hybrid.

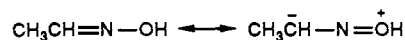
Our recent investigation of the barrier to internal rotation of amides indicated that the carbonyl oxygen was relatively unaffected during rotation about the C-N bond and that the main structural and charge distribution effects were found in the C-N bond.^{3b,7} In the planar form, the nitrogen had a larger electron population than in the 90° rotated form, and the electron population was taken from the carbonyl carbon. These results are not in accord with the simple resonance formulation for the origin of the rotational barrier.

In order to explore the interactions in these systems in further detail, we have examined the conversion of acetaldehyde to its fluorimine (1), to its oxime (2), to its hydrazone (3), and to its methylimine (4):



It is known that imines hydrolyze readily in water, whereas oximes and hydrazones can be formed in its presence.⁴ This implies that

the formation constant for the imine is significantly smaller than that for the other two compounds. One explanation is that oximes are stabilized by a resonance interaction which is not possible with the imines:⁴



In an investigation of the formation constants and their origins, we have calculated the geometries and energies of a number of rotamers of compounds 1-4. The origins of the differences in conformational energies are discussed. The compounds were further examined by calculating the atom properties via numerical integration of the charge density within properly defined atomic regions.

2. Potential Energy Surface Analysis

The potential energy surfaces of *N*-fluoroacetaldimine (1), acetaldoxime (2), acetaldehyde hydrazone (3), and *N*-methylacetaldimine (4) have been examined to determine the configurational and conformational preferences. Each of these molecules is capable of forming various isomers with regard to the configuration about the CN double bond and with regard to the conformation of the acetaldehyde methyl group. Two stereochemical descriptors are used to clearly indicate these stereochemistries. The *E/Z* nomenclature is used to describe the configuration about the CN bond. The second descriptor, eclipsed or staggered, always refers to the conformation of the methyl group with regard to the CN bond. In the cases of 2, 3, and 4, a third stereochemical

(1) Wheland, G. W. *Resonance in Organic Chemistry*; J. Wiley and Sons: New York, 1955.

(2) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York; p 273, and most introductory organic chemistry texts. For a more recent and contrary view, see: Siggel, M. R.; Thomas, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 4360. Thomas, T. D.; Siggel, M. R. F.; Streitwieser, A. *THEOCHEM* **1988**, *108*, 309. Siggel, M. R. F.; Streitwieser, A.; Thomas, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 8022. Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 1872. Wiberg, K. B.; Breneman, C. M.; LePage, T. L. *J. Am. Chem. Soc.* **1990**, *112*, 61. Wiberg, K. B. *J. Am. Chem. Soc.* **1990**, *112*, 4177.

(3) (a) Reference 1, pp 109 and 160. (b) For a contrary view, see: Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1987**, *109*, 5935.

(4) Cf. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 2nd ed.; Plenum Press: New York, 1984; Part A, p 415.

(5) Kemp, D. S.; Vellaccio, F. *Organic Chemistry*; Worth Publishers: New York, 1980; p 811.

(6) Pauling, L.; Wilson, E. B., Jr. *Introduction to Quantum Chemistry*; McGraw-Hill: New York, 1935; pp 159-160.

(7) Wiberg, K. B.; Breneman, C. M. *J. Am. Chem. Soc.*, in press.

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Table I. Total Energies, Vibrational Zero-Point Energies, Relative Energies, and Dipole Moments^{a,b}

| compound ^c | CSS | E(6-31G*) | VZPE | ΔE | ΔH | μ | E(6-31+G*) | ΔE | ΔH | μ |
|--|-----|------------|-------|------------|------------|-------|------------|------------|------------|-------|
| water (C _{2v}) | M | -76.01075 | 14.42 | | | 2.20 | -76.01771 | | | 2.30 |
| fluoroamine (C _s) | M | -154.95578 | 19.10 | | | 2.54 | -154.96611 | | | 2.65 |
| methyl fluoride (C _{3v}) | M | -139.03461 | 26.61 | | | 2.02 | -139.04416 | | | 2.15 |
| hydroxylamine (C _s) | M | -130.97884 | 27.74 | | | 0.68 | -130.98618 | | | 0.71 |
| methanol (C _s) | M | -115.03542 | 34.49 | | | 1.94 | -115.04092 | | | 2.01 |
| hydrazine (C ₂) | M | -111.16937 | 36.44 | | | 2.24 | -111.17645 | | | 2.28 |
| methylamine (C _s) | M | -95.20983 | 43.24 | | | 1.53 | -95.21414 | | | 1.59 |
| acetaldehyde (C _s) | M | -152.91597 | 37.61 | | | 2.98 | -152.92110 | | | 3.21 |
| ethane (D _{3d}) | M | -79.22875 | 50.05 | | | 0.00 | -79.22945 | | | 0.00 |
| <i>N</i> -Fluoroacetaldimine | | | | | | | | | | |
| (<i>E</i> , <i>ecl</i>)-1a | M | -231.86351 | 40.74 | 0.00 | 0.00 | 3.41 | -231.87289 | 0.00 | 0.00 | 3.67 |
| (<i>E</i> , <i>stag</i>)-1b | TS | -231.86040 | 40.51 | 1.95 | 1.74 | 3.41 | -231.86985 | 1.91 | 1.70 | 3.67 |
| (<i>Z</i> , <i>ecl</i>)-1c | M | -231.86258 | 40.87 | 0.58 | 0.69 | 3.40 | -231.87152 | 0.86 | 0.97 | 3.64 |
| (<i>Z</i> , <i>stag</i>)-1d | M | -231.86245 | 40.83 | 0.67 | 0.75 | 3.31 | -231.87166 | 0.77 | 0.83 | 3.55 |
| Acetaldoxime | | | | | | | | | | |
| (<i>E</i> , <i>ecl</i> , <i>trans</i>)-2a | M | -207.88442 | 49.36 | 0.00 | 0.00 | 0.82 | -207.89167 | 0.00 | 0.00 | 0.96 |
| (<i>E</i> , <i>stag</i> , <i>trans</i>)-2b | TS | -207.88133 | 49.11 | 1.94 | 1.71 | 0.85 | -207.88869 | 1.87 | 1.64 | 0.97 |
| (<i>Z</i> , <i>ecl</i> , <i>trans</i>)-2c | M | -207.88319 | 49.51 | 0.77 | 0.91 | 0.77 | -207.89035 | 0.83 | 0.97 | 0.91 |
| (<i>Z</i> , <i>stag</i> , <i>trans</i>)-2d | M | -207.88335 | 49.54 | 0.67 | 0.83 | 0.71 | -207.89077 | 0.56 | 0.72 | 0.85 |
| (<i>E</i> , <i>ecl</i> , <i>cis</i>)-2e | M | -207.87499 | 49.18 | 5.92 | 5.76 | 3.58 | -207.88119 | 6.58 | 6.42 | 3.76 |
| (<i>E</i> , <i>TS</i> NO-rot)-2f | TS | -207.87164 | 48.58 | 8.02 | 7.32 | 3.52 | -207.87842 | 8.31 | 7.61 | 3.69 |
| (<i>E</i> , <i>HONC</i> = 90°)-2g | NS | -207.87346 | | 6.88 | | | -207.88057 | 6.97 | | |
| Acetaldehyde Hydrazone | | | | | | | | | | |
| (<i>E</i> , <i>ecl</i> , <i>perp</i>)-3a | M | -188.07189 | 57.96 | 0.00 | 0.00 | 2.14 | -188.07834 | 0.00 | 0.00 | 2.25 |
| (<i>E</i> , <i>stag</i> , <i>perp</i>)-3b | TS | -188.06900 | 57.71 | 1.81 | 1.58 | 2.11 | -188.07559 | 1.74 | 1.51 | 2.19 |
| (<i>Z</i> , <i>ecl</i> , <i>perp</i>)-3c | TS | -188.06835 | 58.07 | 2.22 | 2.32 | 2.26 | -188.07496 | 2.12 | 2.22 | 2.39 |
| (<i>Z</i> , <i>stag</i> , <i>perp</i>)-3d | M | -188.06990 | 58.25 | 1.25 | 1.51 | 2.24 | -188.07661 | 1.09 | 1.35 | 2.37 |
| (<i>E</i> , <i>ecl</i> , <i>plan.</i>)-3e | TS | -188.06510 | 56.99 | 4.26 | 3.39 | 1.71 | -188.07195 | 4.01 | 3.14 | 1.77 |
| (<i>Z</i> , <i>stag</i> , <i>plan.</i>)-3f | TS | -188.06343 | 57.31 | 5.31 | 4.72 | 2.06 | -188.07076 | 4.76 | 4.17 | 2.19 |
| (<i>E</i> , <i>ecl</i> , <i>cis</i>)-3g | TS | -188.06846 | 57.73 | 2.15 | 1.94 | 0.52 | -188.07564 | 1.69 | 1.48 | 0.65 |
| (<i>E</i> , <i>ecl</i> , <i>trans</i>)-3h | TS | -188.05580 | 57.35 | 10.10 | 9.55 | 3.71 | -188.06262 | 9.86 | 9.31 | 3.86 |
| <i>N</i> -Methylacetaldimine | | | | | | | | | | |
| (<i>E</i> , <i>ecl</i> , <i>ecl</i>)-4a | M | -172.10583 | 65.06 | 0.00 | 0.00 | 1.69 | -172.11013 | 0.00 | 0.00 | 1.83 |
| (<i>E</i> , <i>ecl</i> , <i>stag</i>)-4b | TS | -172.10231 | 64.71 | 2.21 | 1.89 | 1.82 | -172.10678 | 2.10 | 1.78 | 1.96 |
| (<i>E</i> , <i>stag</i> , <i>ecl</i>)-4c | TS | -172.10327 | 64.85 | 1.61 | 1.42 | 1.62 | -172.10767 | 1.54 | 1.35 | 1.77 |
| (<i>E</i> , <i>stag</i> , <i>stag</i>)-4d | S | -172.09962 | 64.49 | 3.90 | 3.39 | 1.75 | -172.10421 | 3.71 | 3.20 | 1.90 |
| (<i>Z</i> , <i>ecl</i> , <i>stag</i>)-4e | TS | -172.09869 | 64.87 | 4.48 | 4.31 | 2.23 | -172.10296 | 4.50 | 4.33 | 2.43 |
| (<i>Z</i> , <i>stag</i> , <i>ecl</i>)-4f | M | -172.09921 | 65.10 | 4.15 | 4.19 | 2.11 | -172.10328 | 4.30 | 4.34 | 2.29 |

^a Abbreviations: CSS = character of stationary structure (M = minimum, TS = transition-state structure, NS = nonstationary structure obtained by constrained optimization, S = second-order saddle point); vibrational zero-point energies (VZPE) are unscaled; relative energies (ΔH) include scaled (factor 0.9) VZPEs. ^b Units: total energies in hartrees, relative energies and VZPEs in kilocalories per mole, and dipole moments in debyes. ^c See text for definition of the stereochemical descriptors.

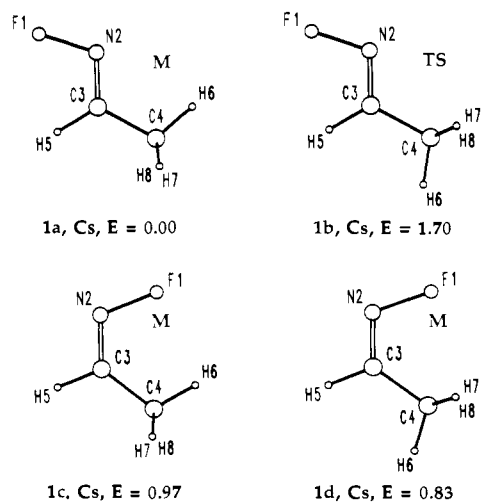


Figure 1. Optimized structures of *N*-fluoroacetaldimine (1). Minima and transition-state structures are marked M and TS, respectively.

descriptor is needed (see below).

We first calculated the geometries and energies of all of the compounds using the 6-31G* basis set.⁸ Since it is known that

Table II. Optimized Structures of *N*-Fluoroacetaldimine (1)^a

| parameter | 1a | 1b | 1c | 1d |
|-------------|--------|--------|--------|--------|
| F1-N2 | 1.374 | 1.374 | 1.375 | 1.376 |
| N2-C3 | 1.251 | 1.250 | 1.252 | 1.252 |
| C3-C4 | 1.495 | 1.504 | 1.496 | 1.500 |
| C3-H5 | 1.079 | 1.077 | 1.077 | 1.076 |
| C4-H6 | 1.082 | 1.082 | 1.078 | 1.082 |
| C4-H7 | 1.085 | 1.083 | 1.085 | 1.083 |
| F1-N2-C3 | 109.51 | 109.52 | 110.99 | 109.75 |
| N2-C3-C4 | 119.77 | 119.70 | 129.13 | 126.77 |
| N2-C3-H5 | 120.15 | 119.80 | 112.29 | 112.83 |
| C3-C4-H6 | 110.68 | 110.38 | 111.79 | 110.60 |
| C3-C4-H7 | 109.16 | 110.58 | 109.41 | 110.20 |
| N2-C3-C4-H7 | 120.76 | 59.89 | 121.32 | 59.34 |

^a Bond distances in angstroms and bond angles in degrees.

lone pairs frequently need diffuse functions in order to give satisfactory wave functions,⁹ the energies and wave functions were then calculated using the 6-31+G* basis set and the 6-31G* geometries. In the case of acetaldehyde, it was shown that the addition of diffuse functions had little effect on the optimized structure. All structures were optimized within the constraints of the symmetry point groups specified in Figures 1-4. Vibrational frequencies were then calculated analytically to characterize

(8) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(9) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294.

Table III. Optimized Structures of Acetaldoxime (2)^a

| parameter | 2a | 2b | 2c | 2d | 2e | 2f | 2g |
|-------------|---------|--------|---------|--------|---------|---------|---------|
| O1-N2 | 1.375 | 1.375 | 1.374 | 1.374 | 1.359 | 1.390 | 1.400 |
| O1-H5 | 0.947 | 0.946 | 0.946 | 0.946 | 0.953 | 0.949 | 0.949 |
| N2-C3 | 1.251 | 1.250 | 1.253 | 1.253 | 1.251 | 1.252 | 1.252 |
| C3-C4 | 1.497 | 1.506 | 1.500 | 1.502 | 1.498 | 1.497 | 1.497 |
| C3-H6 | 1.080 | 1.080 | 1.077 | 1.076 | 1.086 | 1.083 | 1.081 |
| C4-H7 | 1.082 | 1.083 | 1.079 | 1.083 | 1.081 | 1.081 | 1.082 |
| C4-H8 | 1.086 | 1.084 | 1.086 | 1.084 | 1.086 | 1.086 | 1.086 |
| C4-H9 | 1.086 | 1.084 | 1.086 | 1.084 | 1.086 | 1.086 | 1.086 |
| N2-O1-H5 | 104.26 | 104.26 | 103.88 | 104.15 | 110.12 | 107.71 | 105.73 |
| O1-N2-C3 | 111.78 | 111.86 | 113.45 | 112.13 | 117.42 | 113.98 | 112.07 |
| N2-C3-C4 | 120.58 | 120.40 | 128.51 | 126.25 | 120.93 | 120.66 | 120.63 |
| N2-C3-H6 | 120.12 | 119.75 | 113.66 | 114.13 | 121.12 | 120.79 | 120.41 |
| C3-C4-H7 | 110.48 | 110.55 | 111.91 | 110.64 | 110.08 | 110.31 | 110.46 |
| C3-C4-H8 | 110.46 | 110.81 | 109.68 | 108.93 | 110.56 | 110.49 | 110.29 |
| C3-C4-H9 | 110.46 | 110.81 | 109.68 | 108.93 | 110.56 | 110.20 | 110.24 |
| H5-O1-N2-C3 | 180.00 | 180.00 | 180.00 | 180.00 | 0.00 | 61.66 | 90.00 |
| O1-N2-C3-C4 | 180.00 | 180.00 | 0.00 | 0.00 | 180.00 | 178.82 | 178.62 |
| O1-N2-C3-H6 | 0.00 | 0.00 | 180.00 | 180.00 | 0.00 | -0.71 | -0.45 |
| N2-C3-C4-H7 | 0.00 | 180.00 | 0.00 | 180.00 | 0.00 | 0.00 | 0.00 |
| N2-C3-C4-H8 | 120.66 | 59.91 | 121.24 | 59.27 | 120.52 | 120.70 | 120.79 |
| N2-C3-C4-H9 | -120.66 | -59.91 | -121.24 | -59.27 | -120.52 | -120.68 | -120.77 |

^a Bond distances in angstroms and bond angles in degrees.Table IV. Optimized Structures of Acetaldehyde Hydrazone (3)^a

| parameter | 3a | 3b | 3c | 3d | 3e | 3f | 3g | 3h |
|--------------|---------|--------|---------|--------|--------|--------|---------|---------|
| N1-N2 | 1.379 | 1.378 | 1.379 | 1.380 | 1.341 | 1.340 | 1.430 | 1.430 |
| N1-H5 | 1.004 | 1.004 | 1.000 | 1.048 | 0.988 | 0.988 | 1.004 | 1.004 |
| N1-H6 | 0.998 | 0.998 | 0.998 | 0.998 | 0.995 | 0.993 | 1.004 | 1.004 |
| N2-C3 | 1.251 | 1.250 | 1.254 | 1.254 | 1.254 | 1.258 | 1.251 | 1.251 |
| C3-C4 | 1.500 | 1.507 | 1.506 | 1.507 | 1.500 | 1.507 | 1.498 | 1.498 |
| C3-H7 | 1.087 | 1.086 | 1.078 | 1.077 | 1.087 | 1.076 | 1.082 | 1.088 |
| C4-H8 | 1.082 | 1.084 | 1.081 | 1.083 | 1.082 | 1.083 | 1.082 | 1.081 |
| C4-H9 | 1.087 | 1.084 | 1.086 | 1.085 | 1.087 | 1.088 | 1.086 | 1.086 |
| C4-H10 | 1.087 | 1.084 | 1.087 | 1.089 | 1.087 | 1.083 | 1.086 | 1.086 |
| N2-N1-H5 | 112.99 | 112.92 | 113.49 | 112.26 | 116.83 | 116.26 | 105.20 | 108.64 |
| N2-N1-H6 | 108.36 | 108.35 | 107.41 | 107.80 | 122.12 | 123.29 | 105.20 | 108.64 |
| N1-N2-C3 | 118.27 | 118.33 | 120.08 | 118.09 | 119.59 | 120.02 | 112.34 | 117.01 |
| N2-C3-C4 | 121.46 | 121.03 | 129.58 | 126.50 | 121.26 | 126.22 | 121.44 | 121.48 |
| N2-C3-H7 | 121.19 | 120.96 | 114.91 | 115.34 | 121.13 | 115.31 | 120.33 | 121.49 |
| C3-C4-H8 | 110.07 | 110.67 | 113.47 | 110.64 | 110.00 | 110.59 | 110.49 | 110.13 |
| C3-C4-H9 | 110.80 | 110.90 | 109.30 | 110.73 | 111.05 | 111.52 | 110.32 | 110.39 |
| C3-C4-H10 | 110.79 | 110.75 | 110.43 | 111.49 | 111.05 | 111.52 | 110.32 | 110.39 |
| H5-N1-N2-C3 | 30.97 | 31.15 | 38.96 | 45.45 | 180.00 | 180.00 | 125.19 | 58.09 |
| H6-N1-N2-C3 | 152.65 | 152.76 | 159.72 | 163.27 | 0.00 | 0.00 | -125.19 | -58.09 |
| N1-N2-C3-C4 | 177.08 | 176.93 | 0.00 | -1.55 | 180.00 | 0.00 | 180.00 | 180.00 |
| N1-N2-C3-H7 | -2.59 | -2.49 | 178.18 | 177.97 | 0.00 | 180.00 | 0.00 | 0.00 |
| N2-C3-C4-H8 | 0.00 | 180.00 | 2.47 | 169.17 | 0.00 | 180.00 | 0.00 | 0.00 |
| N2-C3-C4-H9 | 120.55 | 59.81 | 122.59 | 48.62 | -59.59 | 60.19 | 120.88 | 120.76 |
| N2-C3-C4-H10 | -120.55 | -59.91 | -119.77 | -71.26 | 59.59 | -60.19 | -120.88 | -120.76 |

^a Bond distances in angstroms and bond angles in degrees.

the stationary structures and to obtain the vibrational zero-point energies. Total energies, relative energies, vibrational zero-point energies, and dipole moments are summarized in Table I. In the following, the energies obtained at the RHF/6-31+G**//RHF/6-31G* level and including the scaled vibrational zero-point energy corrections are discussed unless otherwise noted. Complete sets of structural parameters are listed in Tables II-V.

N-Fluoroacetalimine. For both the *E*- and the *Z*-configured *N*-fluoroacetalimine, two structures were examined in which the methyl group assumes either an eclipsed or a staggered conformation with regard to the CN double bond.¹⁰ The *E*, eclipsed geometry **1a** is the most stable structure of **1**. The *E*, staggered structure **1b** is the transition state for methyl rotation ($E_a = 1.7$ kcal/mol). While we find a distinct conformational preference in the *E* configuration, there exists practically no such preference

in the *Z*-configured isomers. Both the eclipsed and the staggered structures **1c** and **1d**, respectively, are local minima with a very small energetic preference (0.1 kcal/mol) for the latter. The methyl conformation has but small energetic consequences, and there is thus no need to determine the actual transition state for methyl rotation; the methyl rotation is essentially free in the *Z* isomer. The *E* conformer was preferred over *Z* by 0.8 kcal/mol.

Acetaldoxime. The potential energy surface of acetaldoxime is slightly more complicated compared to the one of *N*-fluoroacetalimine due to possible rotamers with respect to the NO bond. The conformers have previously been studied at the RHF/3-21G level of theory.¹¹ In order to be consistent with the other parts of this study, they have been reoptimized at the RHF/6-31G* theoretical level, followed by RHF/6-31+G* single-point energy calculations. The stereochemistry with regard to the NO bond will be described with *cis/trans* nomenclature. Most of the

(10) The inversion barriers for the related *N*-fluoroformimine and formaldoxime have been studied: Bach, R. D.; Wolber, G. J. *J. Org. Chem.* **1982**, *47*, 245. They found that electronegative groups increased the inversion barrier.

(11) Glaser, R.; Streitwieser, A. *J. Am. Chem. Soc.* **1989**, *111*, 7340. See also: Dorigo, A. E.; Pratt, D. W.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6591. Venanzi, T. J.; Venzni, C. A. *J. Comput. Chem.* **1988**, *9*, 67.

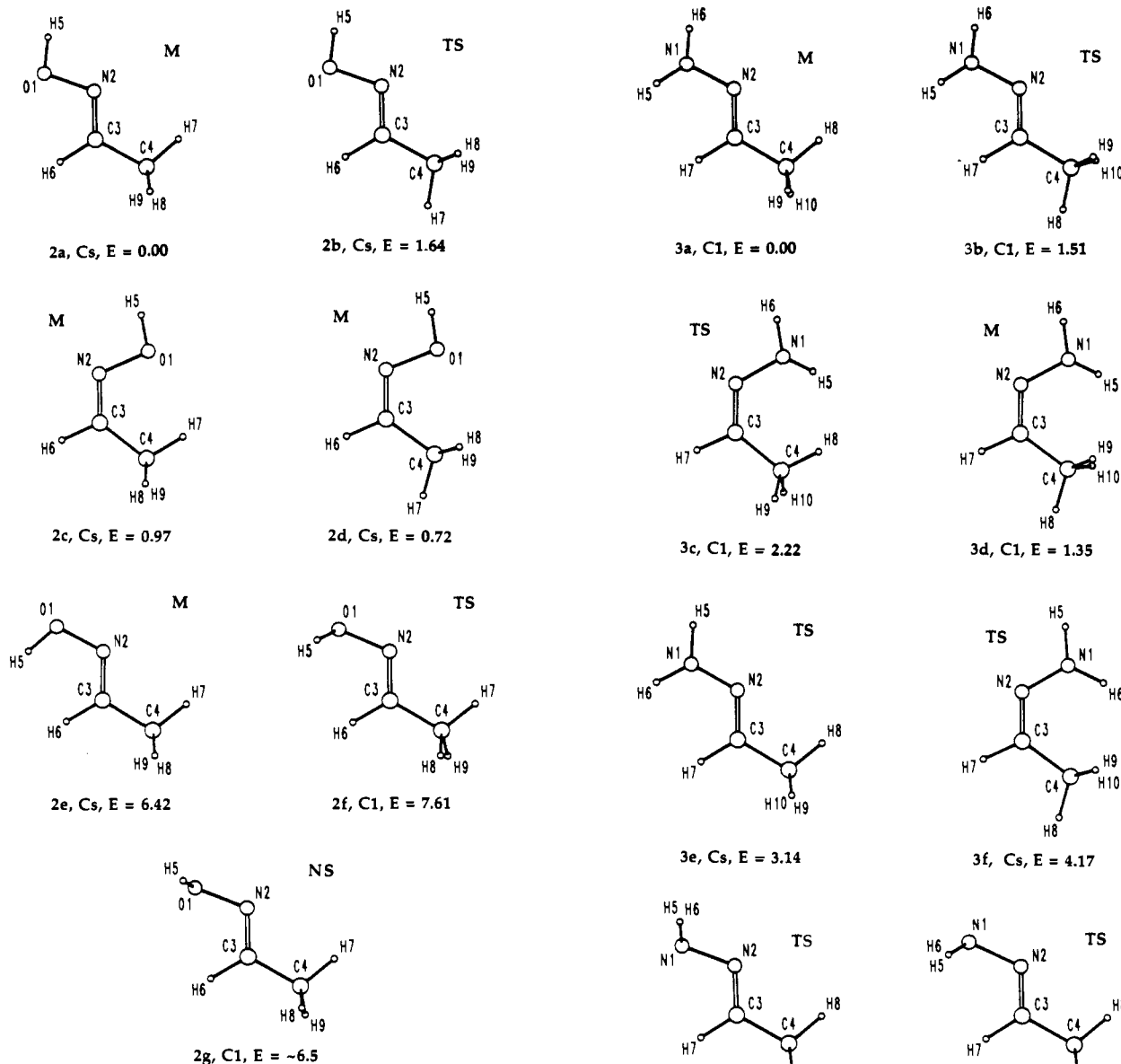


Figure 2. Optimized structures of acetaldoxime (**2**). Compare Figure 1. Structure **2g** is not a stationary structure.

structures examined have the NO trans conformation.

First, we examined the four NO trans structures of **2** that are analogous to the *N*-fluoroacetaldimines **1a-d**. The same pattern was found regarding the stereochemical preferences and also regarding their relative stabilities. The *E*,eclipsed structure **2a** is the most stable minimum, and the staggered structure **2b** is the transition-state structure for the methyl rotation process that requires 1.6 kcal/mol of activation energy. As with **1**, the structures **2c** and **2d** are both minima, and they are almost isoenergetic with only a marginal preference for **2d**. The *E* preference energy is 0.7 kcal/mol for the acetaldoxime (**2**).

The *E*,eclipsed structure **2e** with the NO cis conformation also was examined. Structure **2e** is a minimum on the potential energy surface, but it is 6.4 kcal/mol less stable than the global minimum for **2**, presumably because of repulsion between the electron density associated with the lone pairs on the heteroatoms along with the repulsion between H₅ and H₆. The latter leads to an increase in the N-O-H angle from 104.8° in **2a** to 110.1° in **2e** and results in rehybridization at oxygen. This accounts for the decrease in N-O bond length from 1.375 Å in **2a** to 1.359 Å in **2e**.

The transition-state structure for rotation of the hydroxyl hydrogen around the NO bond is of particular interest for the present discussion. If the classical resonance model were to apply to **2**, then one would expect this rotation to require substantial activation

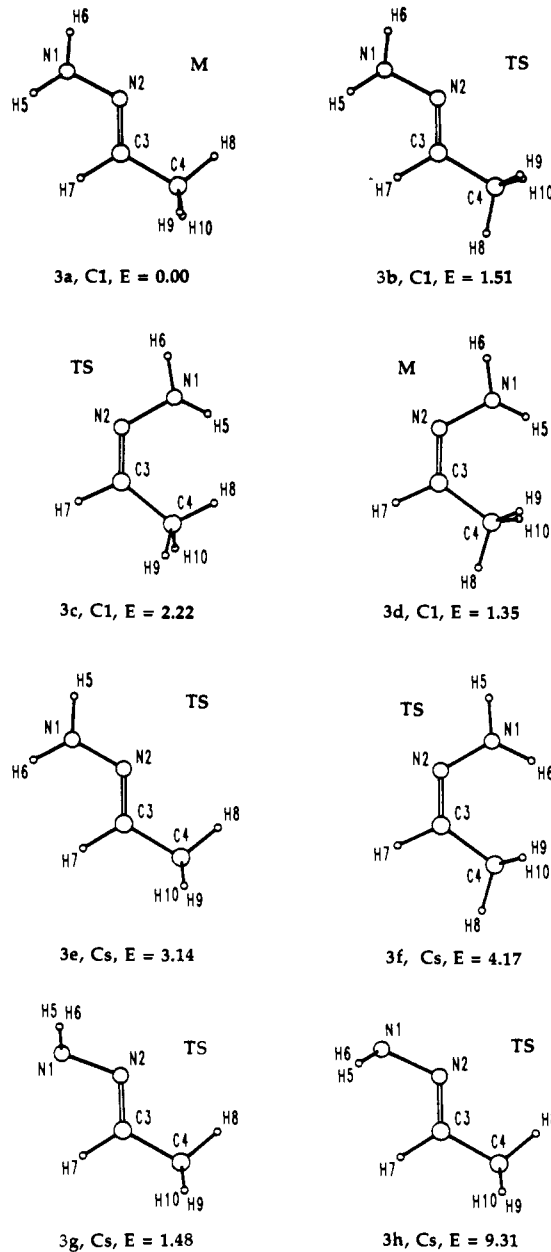


Figure 3. Optimized structures of acetaldehyde hydrazone (**3**).

Table V. Optimized Structures of *N*-Methylacetaldimine (**4**)^a

| parameter | 4a | 4b | 4c | 4d | 4e | 4f |
|--------------|--------|--------|--------|--------|---------|--------|
| C1-N2 | 1.443 | 1.454 | 1.443 | 1.453 | 1.452 | 1.444 |
| C1-H9 | 1.090 | 1.082 | 1.090 | 1.082 | 1.082 | 1.086 |
| C1-H10 | 1.084 | 1.087 | 1.085 | 1.086 | 1.086 | 1.085 |
| N2-C3 | 1.248 | 1.248 | 1.248 | 1.248 | 1.250 | 1.250 |
| C3-C4 | 1.500 | 1.500 | 1.508 | 1.509 | 1.508 | 1.516 |
| C3-H5 | 1.090 | 1.090 | 1.089 | 1.089 | 1.083 | 1.082 |
| C4-H6 | 1.082 | 1.082 | 1.084 | 1.084 | 1.081 | 1.083 |
| C4-H7 | 1.087 | 1.087 | 1.084 | 1.084 | 1.087 | 1.085 |
| N2-C1-H9 | 113.63 | 109.25 | 113.63 | 109.26 | 108.63 | 115.44 |
| N2-C1-H10 | 109.17 | 111.55 | 109.21 | 111.54 | 112.08 | 108.56 |
| C1-N2-C3 | 118.77 | 117.96 | 118.82 | 118.03 | 120.60 | 121.36 |
| N2-C3-C4 | 122.38 | 122.27 | 121.75 | 121.63 | 129.59 | 128.73 |
| N2-C3-H5 | 121.59 | 121.90 | 121.49 | 121.76 | 116.09 | 115.84 |
| C3-C4-H6 | 110.20 | 110.00 | 111.32 | 111.35 | 113.49 | 110.05 |
| C3-C4-H7 | 110.47 | 110.53 | 110.30 | 110.23 | 109.61 | 111.50 |
| H9-C1-N2-C3 | 0.00 | 180.00 | 0.00 | 180.00 | 180.00 | 0.00 |
| H10-C1-N2-C3 | 121.50 | 60.59 | 121.47 | 60.57 | 60.91 | 121.97 |
| C1-C2-C3-C4 | 180.00 | 180.00 | 180.00 | 180.00 | 0.00 | 0.00 |
| N2-C3-C4-H6 | 0.00 | 0.00 | 0.00 | 180.00 | 180.00 | 180.00 |
| N2-C3-C4-H7 | 120.79 | 120.75 | 59.45 | 59.40 | 121.463 | 60.24 |

^a Bond distances in angstroms and bond angles in degrees.

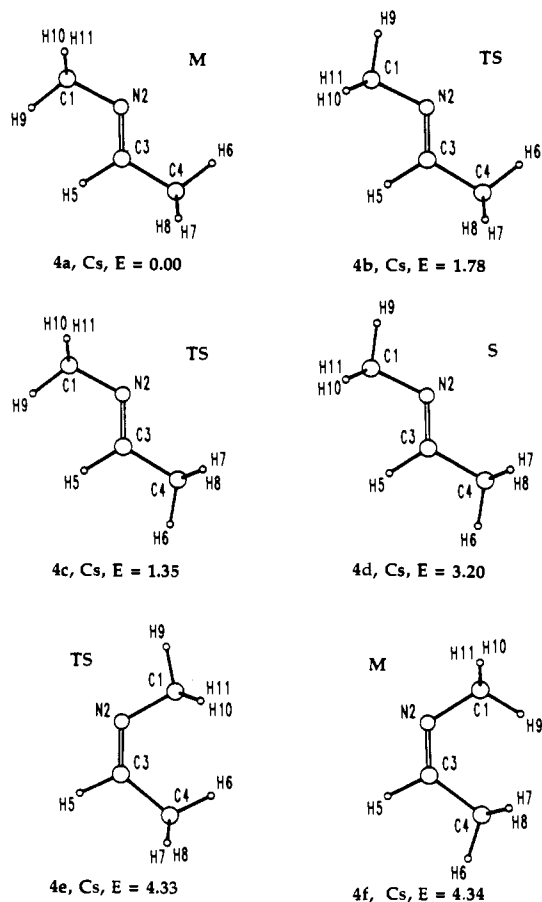


Figure 4. Optimized structures of *N*-methylacetaldimine (**4**). The structure marked by S corresponds to a second-order saddle point on the potential energy surface.

and, furthermore, one might expect a transition structure in which the HO bond axis would be nearly perpendicular to the best plane of the oxime skeleton. Such behavior is not found. The transition-state structure **2f** is only 1.2 kcal/mol less stable than *cis*-NO-**2e** and it is 7.6 kcal/mol less stable than *trans*-NO-**2a**. The dihedral angle H-O-N-C is 61.7° in **2f**. The transition-state structure more closely resembles the less stable structure **2e**, in agreement with Hammond's postulate. We have also considered a structure in which the dihedral angle H-O-N-C was fixed to 90°, and this (nonstationary) structure, **2g**, is 1.3 kcal/mol more stable than **2f** at the RHF/6-31+G* level. Clearly, such a structure would provide the least overlap for resonance interaction, and if the resonance picture were entirely correct, a structure of the type **2g** with a dihedral angle H-O-N-C close to 90° would be expected as the transition-state structure for NO rotation.

The increase in N-O bond length on going from **2a** (1.375 Å) to **2f** (1.390 Å) might also be noted. It probably arises from the lone-pair repulsion in **2f**.

Acetaldehyde Hydrazone. Various conformations of the amine group in the acetaldehyde hydrazone (**3**) have been examined. We describe these conformations with the direction of the axis that bisects the HNH angle and that points from the nucleus in the direction of the nitrogen "lone pair".

The asymmetric hydrazones **3a-d** correspond to the *N*-fluoroacetaldimines **1a-d** and to the acetaldoximes **2a-d** with regard to their CN configurations and methyl conformations. All of these structures have pyramidalized amino groups in which the N lone pair is oriented almost perpendicular to the best plane of the hydrazone skeleton. As with **1** and **2**, the most stable isomer of **3** is the one with the CN *E* configuration and an eclipsing methyl group, **3a**. The conformer in which the methyl group is staggered, **3b**, is the transition-state structure for methyl rotation. The methyl rotation requires 1.5 kcal/mol of activation energy. In the cases of **1** and **2**, we found two nearly isoenergetic local

minima for the *Z* configuration that have the methyl group either in an eclipsed or in a staggered conformation. The hydrazone distinctly differs in this regard: only the staggered methyl conformation **3d** is found to be a minimum and the eclipsed conformation is assumed in the transition-state structure, **3c**, for methyl rotation in *Z*-**3**. The methyl rotation is not nearly as free as in the cases of the corresponding pathways for **1** and **2**; about 0.9 kcal/mol of activation energy is required for the methyl rotation in **3d** via **3c**.

As mentioned previously, all of the structures **3a-d** do have pyramidalized amino groups. While this structural characteristic would still allow for electron delocalization in the fashion suggested by the classical resonance model, it also points up that the energetic advantage of any such electron delocalization is overcompensated for by the stabilization of the amino group as a consequence of assuming an N-hybridization that allows for higher s character. The *C_s* symmetric structures *E*, eclipsed **3e** and *Z*, staggered **3f**, both with planar amino groups, have been optimized, and the analytic computation of the Hessians shows these structures to be the transition-state structures for the racemizations of **3a** and **3d**, respectively. The N-inversions require 3.1 and 2.8 kcal/mol for the *E* and the *Z* isomers, respectively. It can be seen that the hydrazones are quite different than formamide in which the amine group prefers to be planar and has a significant force constant for out-of-plane bending.

The N-N bond length change on going from **3a** (1.379 Å) to **3e** (1.341 Å) results from the change in hybridization at N1 on going from pyramidal to planar. In the latter, the lone-pair electrons are in a p orbital, and the N uses an sp² hybrid to bind to N2. In **2a**, the pyramidal N places the lone pair in an orbital with high s character, and the bond to N2 uses an orbital with high p character. It is well-recognized that increased s character leads to shorter bonds.¹²

The second possible pathway for the racemizations of the chiral minima of **3** involves the rotation of the amino group around the NN bond. Each of these processes might proceed in either of two directions involving structures that have the amino lone pair either transoid or cisoid during racemization. We have explored these possibilities for the most stable *E* isomer of **3**. The *C_s* symmetric structures *E*, eclipsed *cis*-**3g** and *E*, eclipsed *trans*-**3h** were optimized and both were found to be transition-state structures. The racemization of **3a** via NN rotation involving **3g** requires 1.5 kcal/mol of activation; that is, the rotational pathway to racemization is less hindered than the inversion pathway via **3e**. This very small barrier for rotation provides compelling evidence that any resonance stabilization of the hydrazone involving electron donation from the amino N to the CN double bond is essentially insignificant. The racemization pathway via **3h** requires substantially more activation energy, 9.3 kcal/mol, presumably because of the unfavorable alignment of the two N lone pairs in **3h**.

***N*-Methylacetaldimine.** The four *C_s* symmetric *E*-configured structures of **4** were examined in which the two methyl groups either are eclipsed or staggered. Two stereochemical descriptors are thus needed to describe the conformation; the first describes the conformation of the methyl group in the acetaldehyde fragment and the second describes the conformation of the *N*-methyl group.

The *E*-configured isomer in which both of the methyl groups eclipse the CN bond, **4a**, is the global minimum for **4**. Rotation of the *N*-methyl group in **4a** leads to **4b**, and this structure is the transition-state structure for rotation of the *N*-methyl group. The activation barrier for this rotation is 1.8 kcal/mol. The structure **4c** results from **4a** by rotation of the acetaldehyde methyl group, and **4c** is the transition-state structure for that rotational isomerization with an activation barrier of 1.4 kcal/mol. In structure **4d**, both of the methyl groups are staggered with regard to the CN bond; this structure is a second-order saddle point and the displacement vectors associated with the two imaginary frequencies indicate a simultaneous rotation of the methyl groups directed at **4a**. The relative energy of **4d** compared to **4a** is 3.20 kcal/mol, just about the sum of the activation energies required for the

Table VI. Calculated Reaction Energies

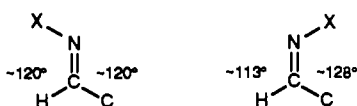
| reaction | energy change (kcal/mol) | | | |
|---|--------------------------|------------|------------|------------|
| | 6-31G* | | 6-31+G* | |
| | ΔE | ΔH | ΔE | ΔH |
| $\text{CH}_3\text{CHO} + \text{H}_2\text{NF} \rightarrow \text{CH}_3\text{CH}=\text{NF}$ (1a) + H_2O | -1.58 | -2.98 | -2.13 | -2.53 |
| $\text{CH}_3\text{CHO} + \text{H}_2\text{NOH} \rightarrow \text{CH}_3\text{CH}=\text{NOH}$ (2a) + H_2O | -0.23 | -1.64 | -1.32 | -2.73 |
| $\text{CH}_3\text{CHO} + \text{H}_2\text{NNH}_2 \rightarrow \text{CH}_3\text{CH}=\text{NNH}_2$ (3a) + H_2O | +1.69 | 0.19 | +0.93 | -0.57 |
| $\text{CH}_3\text{CHO} + \text{H}_2\text{NCH}_3 \rightarrow \text{CH}_3\text{CH}=\text{NCH}_3$ (4a) + H_2O | +5.79 | +4.47 | +4.64 | +3.32 |

individual methyl rotations in **4a**.

In the case of the *Z*-configured **4**, two structures were examined in which one of the methyl groups is in an eclipsed position and the other is in a staggered position. The structure in which the acetaldehyde methyl group is staggered and the other one is eclipsed, **4f**, is a minimum, and **4e**, the structure in which the two methyl conformations are reversed, is the transition-state structure for the narcissistic isomerization of **4f** involving two simultaneous methyl rotations. Both methyl groups have to rotate in a coupled fashion. At the RHF/6-31+G**/RHF/6-31G* level, **4e** is 0.2 kcal/mol more stable than **4f**. However, when the difference of the (scaled) vibrational zero-point energies is taken into account, **4e** and **4f** are found to be virtually isoenergetic.

There is a clear preference for the *E*-configured isomer of **4**: the *E*-configured minimum **4a** is 4.3 kcal/mol more stable than the *Z*-configured minimum **4f**.

Configurational and Conformational Preferences. We find a distinct *energetic preference for the E configuration* in all cases. The *E* preference energies are roughly the same for **1** (0.8 kcal/mol) and **2** (0.7 kcal/mol), about twice as large for **3** (1.4 kcal/mol), and about three times as large for **4** (4.3 kcal/mol). The *E* preference may be ascribed to a steric interaction between the substituents attached to the C=N, as may be seen in the following bond angles:



With the *E* conformer, the angles at the unsaturated carbon are all approximately 120°, whereas in the *Z* conformers the X...C interaction leads to an increase in the angle to ~128°. The magnitude of the conformational preference is also related to the size of the substituent, as indicated by their *A* values.¹³

In all cases, the *E* isomer with the conformation in which the acetaldehyde methyl group is *eclipsed* with regard to the CN bond is energetically favored. The preference energies for the *E*, *eclipsed* isomers over the *E*, *staggered* structures are 1.7 kcal/mol for **1**, 1.6 kcal/mol for **2**, 1.5 kcal/mol for **3**, and 1.4 kcal/mol for **4**; they decrease by about 0.1 kcal/mol each time. In all cases, the *E*, *staggered* stationary structures (**1b**, **2b**, **3b**, **4c**) are the transition-state structures for the rotations of the acetaldehyde methyl groups.

As for the *Z* isomer, a preference for the conformation in which the acetaldehyde methyl group assumes a *staggered* position is found in all cases, but the preference energy with regard to the *eclipsed* structure is very small. This conformational preference energy is only about 0.2 kcal/mol for the *Z*-configured minima of **1** and **2**. While the *eclipsed Z*-configured structures for **1** and **2** are minima, the *eclipsed Z* structure **4f** formally is a transition-state structure, but it becomes essentially isoenergetic with the *staggered* minimum when the vibrational zero-point energies are taken into account. Thus, we conclude that the methyl rotation in *Z*-**4** is essentially free and that these rotations in *Z*-**1** and *Z*-**2** also require very small amounts of activation energy. The hydrazone **3** stands out in that there is a significantly higher barrier (0.9 kcal/mol) for the corresponding rotational process (**3d** to **3d** via **3c**), but it still remains only about half as hindered as the corresponding process in the *E* isomer.

3. Reaction Energies for the Formations of the Imine Derivatives

At the level of optimization (6-31G*), we find the formations of the fluoroimine and of the oxime to be exothermic by 1.58 and 0.23 kcal/mol, respectively, whereas the formations of the hydrazone and of the *N*-methylimine are endothermic by 1.69 and 5.79 kcal/mol, respectively (Table VI). Augmentation of the basis set with diffuse functions has the expected effect: the diffuse functions are most beneficial for the functional description of the acetaldimines formed, and thus, the reaction energies are all made more exothermic or less endothermic at the RHF/6-31+G**/RHF/6-31G* level (-3.0 for **1a**, -1.3 for **2a**, 0.9 for **3a**, and 4.6 for **4a**). The sum of the vibrational zero-point energies of the products of the imine formations is larger than the combined vibrational zero-point energies of the reagents in all cases; that is, the reaction energies become still more exothermic when these zero-point energy corrections are taken into account. At our best level, we find reaction energies of -3.5, -2.7, -0.6, and 3.3 kcal/mol for the formation of **1a**, **2a**, **3a**, and **4a**, respectively.

It can be seen that the reaction energies agree with common experience: the *N*-methylimine formation is found to be endothermic, whereas oxime formation is exothermic. Note that hydrazone formation is found to lie between imine and oxime formation and that the formation of the fluoroimine is the most exothermic reaction. This ordering of the reaction energies is particularly interesting as it strongly suggests that the electronegativity of the atom attached to nitrogen might be the determining factor. If the resonance stabilization in the imine derivatives were the dominant factor, then one would expect that the imine formation would be the most exothermic for the imine derivative that is most capable of donating electron density to the CN double bond. On this basis, one would expect just the *opposite* ordering for the reaction energies.

4. Bond and Atom Properties

In order to gain information concerning the nature of the interactions in the molecules and the origin of the differences in energies of reactions and in rotational barriers, we have analyzed the wave functions in detail. Here, we make use of Bader's theory of atoms in molecules.¹⁴ This analysis requires that we first locate the bond critical points for each of the molecules. The bond critical point is the point in the bonding region that represents a minimum in charge density along the bond and a maximum in charge density perpendicular to the bond. The locations of the bond critical points are described by the parameters r_A , r_B , and R , and their values are given in Tables A-D in the supplementary material for the stationary structures of **1-4** and in Table E for the reagents. Each bond critical point is further characterized by the value of the electron density at this point, ρ_c , by the three curvatures, λ_i , and by the ellipticity, ϵ , of the bond.

The location of the bond critical point between a pair of bonded atoms is related to the relative electronegativity of the atoms.¹⁵ In the case of a symmetrical bond, such as in ethane, the bond critical point will be at the midpoint of the bond. With an unsymmetrical bond, such as the C-N bond of methylamine, the greater electronegativity of the nitrogen will result in a charge shift from carbon to nitrogen. The point of minimum charge density along the bond will now move toward the carbon. For

(14) Bader, R. F. W. *Atoms in Molecules. A Quantum Theory*; Oxford University Press: Oxford, 1990.

(15) Bader, R. F. W.; Beddall, P. M.; Cade, P. E. *J. Am. Chem. Soc.* **1971**, *93*, 3095. Boyd, R. J.; Edgecombe, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 4182.

(13) Hanack, M. *Conformation Theory*; Academic Press: New York, 1965; p 103.

Table VII. Atom Properties of *N*-Fluoroacetaldimine (1)

| | 1a | | 1b | | 1c | | 1d | |
|-----------------|---------|--------|---------|--------|---------|--------|---------|--------|
| | n_π | n_T | n_π | n_T | n_π | n_T | n_π | n_T |
| F1 | 1.995 | 9.470 | 1.995 | 9.469 | 1.992 | 9.477 | 1.993 | 9.478 |
| N2 | 1.423 | 7.667 | 1.424 | 7.670 | 1.423 | 7.658 | 1.424 | 7.660 |
| C3 | 0.596 | 5.120 | 0.594 | 5.121 | 0.604 | 5.121 | 0.603 | 5.124 |
| C4 | 0.944 | 5.907 | 0.961 | 5.912 | 0.943 | 5.918 | 0.963 | 5.911 |
| H5 | 0.016 | 0.918 | 0.016 | 0.917 | 0.019 | 0.930 | 0.019 | 0.926 |
| H6 | 0.022 | 0.960 | 0.024 | 0.990 | 0.022 | 0.940 | 0.024 | 0.992 |
| H7 | 0.502 | 0.981 | 0.492 | 0.964 | 0.498 | 0.978 | 0.487 | 0.956 |
| total | 6.000 | 32.004 | 5.998 | 32.006 | 6.000 | 32.001 | 6.001 | 32.002 |
| CH | 0.612 | 6.038 | 0.610 | 6.078 | 0.623 | 6.051 | 0.622 | 6.050 |
| CH ₃ | 1.970 | 8.828 | 1.969 | 8.830 | 1.961 | 8.814 | 1.961 | 8.814 |

this C–N bond, the ratio of the distances from the atoms to the bond critical point is 1.76, favoring nitrogen. Similarly, with the O–N bond of hydroxylamine, the ratio is 1.25, favoring oxygen. The distances from the hydrogens to the bond critical points will always be small because of the small size of the hydrogen. Carbon and hydrogen have similar electronegativities, and the ratio of the distances to the bond critical point for a C–H bond in methylamine is 1.7. For the N–H bonds of methylamine it increases to 2.9, and when the electronegativity of nitrogen is increased, as in hydroxylamine, the ratio further increases to 4.3. Finally, with the O–H bond of water it is 5.6.

The charge density, ρ_c , at the bond critical point is related to the bond order, and it is found to be significantly larger for the double bonds than for the corresponding single bonds. The second derivatives of ρ at the bond critical point (λ_1 , λ_2 , and λ_3) indicate how rapidly ρ changes on moving away from the critical point. For a normal single bond, such as the C–C bond in ethane, the two negative curvatures are equal, but if there is a π -bond, one curvature (in the direction of the π -bond) will be much smaller than the other. This difference may be described by the ellipticity of the bond, which is defined as $\epsilon = \lambda_1/\lambda_2 - 1$. The values of ϵ for the C=N bonds in **1a**, **2a**, **3a**, and **4a** are 0.264, 0.312, 0.367, and 0.269, respectively, and are typical values for double bonds.

Table VIII. Atom Properties of Acetaldoxime (2)

| | 2a | | 2b | | 2c | | 2d | | 2e | | 2f | 2g |
|-----------------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|--------|--------|
| | n_π | n_T | n_π | n_T | n_π | n_T | n_π | n_T | n_π | n_T | n_T | n_T |
| C4 | 0.938 | 5.912 | 0.953 | 5.915 | 0.936 | 5.934 | 0.958 | 5.925 | 0.936 | 5.905 | 5.912 | 5.916 |
| H7 | 0.022 | 0.973 | 0.024 | 1.003 | 0.022 | 0.950 | 0.024 | 1.005 | 0.022 | 0.964 | 0.963 | 0.965 |
| H8 | 0.510 | 0.995 | 0.500 | 0.979 | 0.506 | 0.992 | 0.494 | 0.968 | 0.511 | 0.995 | 0.994 | 0.993 |
| H9 | 0.510 | 0.005 | 0.500 | 0.979 | 0.506 | 0.992 | 0.494 | 0.968 | 0.511 | 0.995 | 0.995 | 0.989 |
| C3 | 0.641 | 5.117 | 0.640 | 5.114 | 0.650 | 5.117 | 0.650 | 5.130 | 0.683 | 5.130 | 5.105 | 5.093 |
| H6 | 0.018 | 0.947 | 0.019 | 0.945 | 0.022 | 0.958 | 0.022 | 0.954 | 0.021 | 0.996 | 0.966 | 0.948 |
| N2 | 1.400 | 7.809 | 1.400 | 7.811 | 1.402 | 7.803 | 1.401 | 7.801 | 1.362 | 7.755 | 7.809 | 7.831 |
| O1 | 1.954 | 8.868 | 1.954 | 8.867 | 1.950 | 8.875 | 1.950 | 8.877 | 1.946 | 8.830 | 8.854 | 8.863 |
| H5 | 0.003 | 0.387 | 0.008 | 0.387 | 0.006 | 0.385 | 0.008 | 0.385 | 0.008 | 0.424 | 0.406 | 0.399 |
| total | 5.996 | 32.002 | 5.999 | 32.000 | 6.000 | 32.006 | 6.001 | 32.013 | 5.999 | 31.994 | 32.000 | 31.997 |
| OH | 1.957 | 9.255 | 1.962 | 9.254 | 1.956 | 9.260 | 1.958 | 9.262 | 1.954 | 9.254 | 9.259 | 9.262 |
| CH | 0.659 | 6.064 | 0.659 | 6.068 | 0.672 | 6.075 | 0.672 | 6.084 | 0.703 | 6.126 | 6.068 | 6.041 |
| CH ₃ | 1.980 | 8.875 | 1.978 | 8.876 | 1.970 | 8.868 | 1.970 | 8.866 | 2.178 | 8.859 | 8.863 | 8.863 |

Table IX. Atom Properties of Acetaldehyde Hydrazone (3)

| | 3a | 3b | 3c | 3d | 3e | | 3f | | 3g | | 3h | |
|-----------------|--------|--------|--------|--------|---------|--------|---------|--------------------|---------|--------|---------|--------|
| | n_T | n_T | n_T | n_T | n_π | n_T | n_π | n_T | n_π | n_T | n_π | n_T |
| C4 | 5.913 | 5.912 | 5.971 | 5.961 | 0.930 | 5.909 | 0.962 | 6.958 ^a | 0.934 | 5.930 | 0.933 | 5.925 |
| H8 | 0.974 | 1.013 | 1.003 | 0.996 | 0.023 | 0.979 | 0.023 | 0.979 | 0.022 | 0.972 | 0.022 | 0.963 |
| H9 | 1.006 | 0.987 | 0.987 | 0.977 | 0.519 | 1.010 | 0.514 | 1.002 | 0.509 | 0.997 | 0.509 | 0.997 |
| H10 | 1.006 | 0.983 | 0.995 | 1.003 | 0.519 | 1.010 | 0.514 | 1.002 | 0.509 | 0.997 | 0.509 | 0.997 |
| C3 | 5.114 | 5.113 | 5.113 | 5.115 | 0.743 | 5.150 | 0.755 | 5.156 | 0.583 | 5.059 | 0.611 | 5.073 |
| H7 | 1.003 | 1.001 | 0.974 | 0.968 | 0.023 | 1.012 | 0.027 | 0.972 | 0.017 | 0.953 | 0.019 | 0.996 |
| N2 | 8.022 | 8.023 | 8.018 | 8.008 | 1.362 | 7.956 | 1.356 | 7.932 | 1.424 | 8.096 | 1.378 | 8.063 |
| N1 | 7.746 | 7.744 | 7.756 | 7.762 | 1.846 | 7.856 | 1.833 | 7.865 | 1.343 | 7.758 | 1.330 | 7.737 |
| H5 | 0.626 | 0.626 | 0.622 | 0.619 | 0.018 | 0.542 | 0.017 | 0.543 | 0.330 | 0.617 | 0.335 | 0.625 |
| H6 | 0.591 | 0.591 | 0.590 | 0.590 | 0.018 | 0.576 | 0.020 | 0.570 | 0.330 | 0.617 | 0.335 | 0.625 |
| total | 32.000 | 31.994 | 32.029 | 31.999 | 6.001 | 32.000 | 5.999 | 32.000 | 5.999 | 31.995 | 6.001 | 32.002 |
| NH ₂ | 8.900 | 8.961 | 8.967 | 8.971 | 1.882 | 8.974 | 1.871 | 8.978 | 2.002 | 8.993 | 2.001 | 8.988 |
| CH | 6.117 | 6.115 | 6.087 | 6.083 | 0.766 | 6.162 | 0.782 | 6.128 | 0.600 | 6.011 | 0.629 | 6.069 |
| CH ₃ | 8.963 | 8.895 | 8.955 | 8.937 | 1.991 | 8.908 | 1.990 | 8.962 | 1.973 | 8.895 | 1.973 | 8.882 |

^aC4 and H8.

The ellipticity of the adjacent X–N bonds for the above compounds are 0.113, 0.014, 0.064, and 0.021, respectively, and the latter three values are quite small, suggesting little π -character in these bonds.

The bond critical points play a special role in that the surfaces that separate pairs of atoms always pass through these points.¹⁴ The surface is generated by starting at a critical point and developing paths along which the charge density decreases most rapidly. A set of these paths, starting in different directions from the bond critical point, forms a partitioning surface. The set of these surfaces, one for each pair of bonded atoms, serves to separate a molecule into a set of volume elements, each of which "belongs" to one of the atoms in the molecule.

Within each of these volume elements, the virial theorem is locally satisfied.¹⁴ Integration of the charge density within a region gives the electron population for the given atom. At the same time, the kinetic energy and other properties of the atom may be calculated in a similar fashion. The data obtained in this fashion are summarized in Tables F–I in the supplementary material for the molecules 1–4 and in Table J for the reagents. Here, the total electron population and, of particular interest in the present context, the π -populations are given first (n_T and n_π) followed by L , which is a measure of the accuracy of the integration for the kinetic energy. The next entry, T , is the integrated kinetic energy of the electrons associated with the given atom, and the value $-E$ is the atom total energy derived from T by correcting for the virial defect of the SCF wave function. The electron populations (both n_T and n_π) for the compounds 1–4 also are summarized in Tables VII–X.

Topological Properties. The electronegativity of the X group affects the location of the N–X bond critical point rather significantly and in the expected direction. In Figure 5, the distances (in angstroms) between the X atom and the N–X bond critical points determined for **1a–4a** (0.812 for F, 0.768 for O, 0.690 for NH₂, and 0.503 for CH₃) are plotted versus the electronegativities of X (F 3.98, O 3.44, N 3.04, and C 2.55). Fluorine and oxygen cause the critical point to be moved rather close to the imine N,

Table X. Atom Properties of *N*-Methylacetaldimine (4)

| | 4a | | 4b | | 4c | | 4d | | 4e | | 4f | |
|--------------------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|
| | n_x | n_T | n_x | n_T | n_x | n_T | n_x | n_T | n_x | n_T | n_x | n_T |
| C1 | 0.912 | 5.471 | 0.902 | 5.501 | 0.912 | 5.469 | 0.903 | 5.498 | 0.898 | 5.497 | 0.912 | 5.483 |
| H9 | 0.024 | 1.033 | 0.022 | 0.998 | 0.024 | 1.033 | 0.023 | 0.998 | 0.023 | 0.997 | 0.027 | 1.031 |
| H10 | 0.513 | 0.996 | 0.520 | 1.010 | 0.513 | 0.996 | 0.521 | 1.011 | 0.521 | 1.012 | 0.510 | 0.994 |
| N2 | 1.430 | 8.544 | 1.428 | 8.527 | 1.432 | 8.547 | 1.431 | 8.530 | 1.429 | 8.520 | 1.428 | 8.531 |
| C3 | 0.613 | 5.046 | 0.610 | 5.043 | 0.611 | 5.043 | 0.606 | 5.035 | 0.612 | 5.031 | 0.617 | 5.038 |
| H5 | 0.020 | 1.006 | 0.020 | 1.008 | 0.020 | 1.004 | 0.020 | 1.006 | 0.210 | 0.985 | 0.021 | 0.983 |
| C4 | 0.930 | 5.932 | 0.930 | 5.932 | 0.951 | 5.934 | 0.952 | 5.934 | 0.941 | 5.965 | 0.942 | 5.963 |
| H6 | 0.022 | 0.973 | 0.022 | 0.972 | 0.025 | 1.016 | 0.025 | 1.016 | 0.026 | 0.998 | 0.024 | 1.002 |
| H7 | 0.512 | 1.003 | 0.512 | 1.003 | 0.500 | 0.982 | 0.500 | 0.981 | 0.504 | 0.992 | 0.505 | 0.991 |
| total | 6.000 | 32.001 | 5.998 | 32.007 | 6.001 | 32.002 | 6.002 | 32.000 | 6.000 | 32.000 | 6.000 | 31.999 |
| (N)CH ₃ | 1.961 | 8.495 | 1.964 | 8.519 | 1.962 | 8.494 | 1.967 | 8.517 | 1.963 | 8.518 | 1.959 | 8.500 |
| CH | 0.633 | 6.052 | 0.630 | 6.051 | 0.631 | 6.047 | 0.626 | 6.041 | 0.633 | 6.016 | 0.638 | 6.021 |
| (C)CH ₃ | 1.975 | 8.911 | 1.976 | 8.910 | 1.976 | 8.914 | 1.977 | 8.912 | 1.975 | 8.946 | 1.976 | 8.947 |

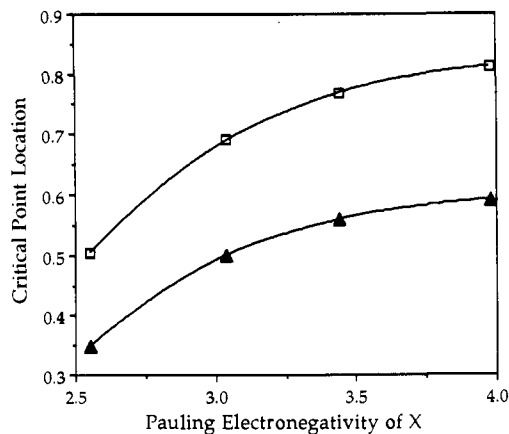


Figure 5. Effect of electronegativity of the imine substituent on the location of the N-X bond critical point shown in two ways. The graph depicted with the squares shows the distance of the critical point from the X atom in absolute value, and the graph depicted with the triangle correlates the F values—a relative measure that reflects N-X bond length differences—with the electronegativities.

the critical point of the N-N bond in **3a** is nearly in the center of the bond, and the critical point is displaced toward the methyl carbon in **4a**. These shifts of the critical points are also reflected in the R values given in the tables. A correlation between the electronegativities and the relative displacement of the critical point from the center of the bond that accounts for the different overall N-X bond lengths might be given using the parameter F , which is defined as the ratio between the distance between the atom X and the N-X critical point and the bond length. The correlation between the F values and the electronegativities also is shown in Figure 5. Both methods yield the same conclusion: *The more electronegative the imine N substituent is, the more its basin extends into the X-N bonding region.*

Integrated Properties. The integration of the electron densities within the basins of the substituents on the imine N result in the charges of -0.47 for F, -0.26 for OH, 0.04 for NH₂, and 0.50 for CH₃ for the most stable isomers of molecules **1-4** (Tables VII-X). In Figure 6, the total electron populations of the groups F, OH, NH₂, and CH₃ are plotted versus the Pauling electronegativities of the heteroatoms. As can be seen, the populations are correlated directly with the electronegativities. Of particular interest are the π -components of these populations. According to the resonance model, one would expect to find a π -population of the substituent that is smaller than 2 because of electron donation toward the double bond. No such π -electron-density transfer is found; the π -populations of the substituent groups in **1a-4a** are all rather close to 2 with only negligible variations.

The atomic charges for the nitrogen and its substituent in the NX groups are summarized in Table XI. Here the total charge and the π -component of the charge are given for X = F, OH, and CH₃. The π -charge is not given for X=NH₂ since the amino group is nonplanar and σ and π cannot be separated. It can be

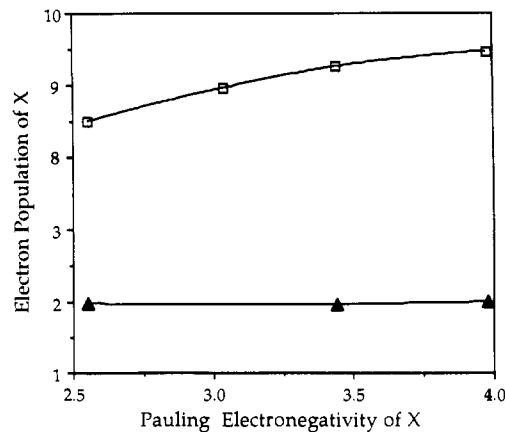


Figure 6. Plot of the electron population of X versus the electronegativity of the heteroatoms. The squares show the total populations and the triangles show the π -components of the populations.

Table XI. Atomic Charges for the NX Groups

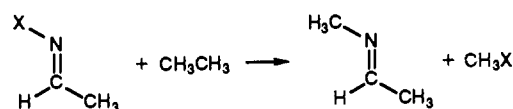
| | X = F | X = OH | X = NH ₂ | X = CH ₃ |
|--------------------------------|-------|--------|---------------------|---------------------|
| X charge | -0.47 | -0.26 | +0.04 | +0.50 |
| X π -charge | 0.00 | +0.03 | | +0.04 |
| N charge | -0.67 | -0.81 | -1.02 | -1.54 |
| N π -charge | -0.42 | -0.40 | | -0.43 |
| NX charge | -1.14 | -1.07 | -0.98 | -1.04 |
| NX π -charge | -0.42 | -0.37 | | -0.39 |
| av NX charge = 1.06 \pm 0.08 | | | | |

seen that whereas the X π -charge is negligible in all cases, the total charge varies considerably with structure. The changes in N and X are in opposite directions, and the total NX charges are essentially independent of X. The relative stability increases as the X and N charges become more equal, suggesting that charge equalization may be an important component of energetic stabilization.

In summary, the data obtained in this investigation show that resonance stabilization is not of importance for any of the compounds **1-4**. The differences in formation constants are related to the electronegativities of the substituents, X, and not to the availability of the lone-pair electrons on the substituents.

5. Origin of the Energy Differences

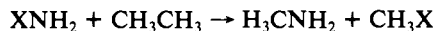
The importance of electronegativity in determining the formation constants for **1-4** suggested an examination of its effect on the energies of the reactants and of the products. This may be done using homoisodesmic reactions such as the following:



An exothermic reaction would indicate that the substituent, X, would prefer to be bonded to methyl rather than to the imine

nitrogen. Using the 6-31+G* energies, the energy changes were as follows: X = F, -32.6 kcal/mol; X = HO, -24.7 kcal/mol; and X = NH₂, -14.0 kcal/mol. Thus, it appears that there is no special stabilization associated with **1**.

Using similar reactions for the reactants,



the energy changes were as follows: X = F, -39.4 kcal/mol; X = HO, -18.8 kcal/mol; and X = NH₂, -10.3 kcal/mol. It can be seen that the preference for the formation of **1** over **4** results from the greater destabilization of fluoroamine as compared to *N*-fluoroacetaldimine.

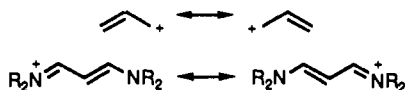
What is the origin of the energy changes for the reactants? It is well-known that bond strength generally increases with increasing differences in electronegativity between the atoms that are joined.¹⁶ Thus, in the series methylamine, methanol, and methyl fluoride, the MeX bond dissociation energies are 84.9, 92.7, and 109.9 kcal/mol.¹⁷ In the absence of other effects, one might expect a similar, although smaller, change in bond dissociation energies for the ammonia derivatives. The H₂NX bond dissociation energies may be estimated from the energies of the isodesmic reactions, the dissociation energies for the methyl compounds, and that for ethane (90.2 kcal/mol). They are as follows: FNH₂, 65.2 kcal/mol; HONH₂, 68.6 kcal/mol; and H₂NNH₂, 69.3 kcal/mol. The value thus estimated for hydrazine is in reasonable agreement with the experimental value, 66 ± 2 kcal/mol.¹⁷ The relative order of the dissociation energies is the opposite of that for the methyl derivatives and clearly is not related to electronegativity. It is likely that the change with respect to the methyl derivatives results from lone-pair repulsions. It is well-recognized that the low bond dissociation energy for fluorine (38 kcal/mol) results from such an interaction,¹⁸ and a similar but weaker interaction would be expected for fluoroamine. The lone-pair repulsion should decrease on going from fluoroamine to hydroxylamine and hydrazine, corresponding to the decrease in the number of lone pairs, and this would account for the order of dissociation energies.

The imines are less basic than the amines, and so the lone pairs of the imines may be contracted somewhat and may give somewhat smaller lone-pair repulsion than the amines. This would account for the less negative isodesmic reactions found with the imines as compared to the amines. Although it is difficult to test this hypothesis, it is clear that the use of such isodesmic reactions in order to estimate other quantities, such as resonance interactions,¹⁹ are subject to large uncertainties resulting from changes in bond energies with changes in substituents.

6. Under What Conditions Will π -Electron Delocalization Have Energetic Consequences?

Cyclic molecules in which the π -electrons occupy closed-shell configurations and may be distributed approximately one per σ -bond always show thermochemical stabilization. An important factor is the reduction in π -electron repulsion as compared to ordinary double bonds in which two π -electrons share one σ -bond.²⁰

With acyclic molecules, the same π -electron distribution may be found in electron-deficient cases for which two equivalent resonance structures may be drawn. Two examples are the allyl cation and the polymethinium dyes:



(16) Pauling, L. *The Nature of the Chemical Bond*, 2nd ed.; Cornell University Press: Ithaca, NY, 1944; p 48.

(17) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

(18) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley: New York, 1988; p 547.

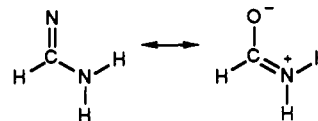
(19) George, P.; Bock, C. W.; Trachtman, M. In *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: Deerfield Beach, FL, 1987; Vol. 4, pp 163ff.

(20) Dewar, M. J. S.; Schmeising, H. N. *Tetrahedron* **1959**, *5*, 166; **1960**, *11*, 96.

Here, the π -electrons are distributed one per σ -bond and, in addition, are more strongly bound because of the overall positive charge. With the allyl cation, the stabilization is on the order of 25 kcal/mol.²¹ The addition of two electrons to the allyl cation giving allyl anion will serve to increase the π -electron repulsion and will lead to a markedly lower stabilization.²² A study of heterosubstituted allyl anions showed that the energy differences could be accounted for by considering only the electronegativity of the terminal atoms, and resonance stabilization appeared to be minimal.¹⁸ The same was found to be the case with the compounds described as having "Y-aromaticity".²³ Here, the electron-deficient trimethylenemethane derivatives were found to have π -electron stabilization, but the corresponding anionic species (trimethylenemethane dianion) and guanidine were found to have little, if any, π -electron stabilization.^{19,24}

In general, it is found that species in which electrons can be delocalized into π -electron-deficient regions (i.e., the delocalization of CH and CC bond electrons into the empty p orbital of carbocations, the delocalization of the double bond electrons into an empty p orbital in allyl cations, and the delocalization of double bond electrons in Kekule structures of aromatic compounds into the adjacent C-C single bond regions) lead to π -electron stabilization. On the other hand, no such regions are present in allyl anions, carbanions, and similar species, and π -electron stabilization should be minimal. These species may, however, be stabilized in the gas phase by charge polarization or other effects which serve to spread out charge and decrease electrostatic energies. In this way, the *tert*-butoxide ion is stabilized over methoxide ion in the gas phase, whereas the opposite order of stability is found in solution.²⁵ Similarly, the 90° (unconjugated) allyl anion will be less stable than the planar allyl anion since the charge is spread out over a larger volume element in the latter.

Formamide is an interesting case since it has a fairly large barrier to rotation about the C-N bond which has been ascribed to double bond character introduced by the zwitterionic resonance structure:



However, we have shown that the oxygen does not participate in the rotation about the C-N bond and that all of the effects are local to that bond.^{3b,7} The large difference in electronegativity between C and O leads to a highly polarized carbonyl group with a rather electron-deficient carbon. In the planar form, the nitrogen chooses to place its lone-pair electrons in a p orbital so that they can interact with the electron-deficient carbon. In doing so, it uses sp² hybrid orbitals to form the bond to carbon. With respect to the saddle point conformer, the N will be more electronegative for two reasons: (a) it has transferred some π -density to carbon and (b) it uses an orbital with higher s character. The increased electronegativity leads to a shift in the bond critical point toward carbon, and in this way the nitrogen acquires charge density from carbon via the σ -system and has a net gain in charge density at the expense of the carbon. The only role of the oxygen is to polarize the C-O bond, making the interaction possible.

With the present compounds, the same type of resonance structures may be written, but again there is no evidence for resonance stabilization. A major difference between formamide and the compounds **1-4** is that, in the latter, the atom next to the heterocenter is not electron deficient and there is not the possibility of an interaction such as is found with formamide. As a result,

(21) Mayr, H.; Forner, W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 6032.

(22) Wiberg, K. B.; Breneman, C. M.; LePage, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 61.

(23) Wiberg, K. B. *J. Am. Chem. Soc.* **1990**, *112*, 4177.

(24) Frenking, G.; Gobbi, A. *Angew. Chem.*, in press.

(25) Bartmess, J. E.; Scott, J. A.; McIver, R. T., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 6046.

no important π -interactions should be expected, and none were found. The major effect contributing to energy differences appeared to be lone-pair repulsion.

7. Calculations

The ab initio calculations were carried out using GAUSSIAN-86,²⁶ and the charge density analysis was performed using PROAIM.²⁷

(26) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R. A.; Whiteside, R. A.; Fox, D. J.; Fluder, E. M.; Pople, J. A. Carnegie-Mellon Quantum Chemistry Publishing Unit, Pittsburgh, PA, 1984.

Acknowledgment. This investigation was supported by grants from the National Institutes of Health and the Exxon Educational Foundation.

Registry No. 1, 137695-67-1; 2, 107-29-9; 3, 5799-73-5; 4, 6898-67-5; CH₃CHO, 75-07-0; NH₃F, 15861-05-9; NH₂OH, 7803-49-8; NH₂NH₂, 302-01-2; CH₃NH₂, 74-89-5.

Supplementary Material Available: Tables A-J listing the bond and atom properties of compounds 1-4 and the compounds from which they are formed (30 pages). Ordering information is given on any current masthead page.

(27) Biegler-König, F. W.; Bader, R. F. W.; Tang, T.-H. *J. Comput. Chem.* 1982, 3, 317.

Molecular Mechanical Investigations of the Properties of Oxocarbenium Ions. 1. Parameter Development[§]

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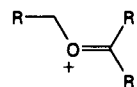
Contribution from the Laboratory for Molecular Modeling, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, and Burroughs Wellcome Company, 3030 Cornwallis Road, Research Triangle Park, North Carolina 27709. Received April 17, 1991

Abstract: The structural properties of a series of acyclic oxocarbenium ions containing the C—O=C atomic linkage have been investigated at the Hartree-Fock and Møller-Plesset ab initio levels with a variety of basis sets up to the 6-311++G** level. The results from the ab initio calculations provide insight into the extent of charge delocalization in these ions, and have been used to generate parameters for the MM2(87) molecular mechanics program. Two approaches to the incorporation of electrostatic interactions within a molecular mechanical framework are presented and evaluated. An application of the parameter set in the evaluation of the relative stabilities and heats of formation of several experimentally observed acyclic oxocarbenium ions is presented.

While oxocarbenium ions are believed to be reaction intermediates in the acid-catalyzed hydrolysis of glycosides,² and ketals in general,³ the transient nature of these species has prevented their isolation. In the case of glycoside hydrolysis, the postulate that the rates of hydrolysis are related to the stabilities of the cyclic oxocarbenium ions has been generally accepted for over 30 years,^{2,4} despite the lack of direct evidence that such a relationship exists. Recently, the importance of nonsteric interactions has been discussed by Toullec,⁵ who reported that C-H acidities in acyclic oxocarbenium ions play a role in determining the rates of hydrolysis of the parent acetals. In contrast, Amyes and Jencks have reported that in the hydrolysis of certain acetals the lifetimes of the oxocarbenium ions may be too short to support the belief that these ions exist as discrete intermediates.⁶

In an effort to quantify the extent to which steric effects are related to oxocarbenium ion stabilities, we have examined the structural properties of a series of closely related oxocarbenium ions, applying computational methods. As we wished to be able to extend the calculational method to larger oxocarbenium ions, derived from oligosaccharides, we chose to treat the problem within a molecular mechanical framework, employing the program MM2(87).⁷ This version of MM2 includes parameters necessary to describe the relationship between C—O—C—O torsion angles and C—O bond lengths as manifest by the anomeric effect.⁸ Among the improvements present in MM2(87) is an ability to describe hydrogen bonding, a feature of particular relevance to carbohy-

Chart I



- 1: R = R' = R'' = H
- 2: R = R' = H, R'' = CH₃
- 3: R = R'' = H, R' = CH₃
- 4: R = H, R' = R'' = CH₃
- 5: R = R' = H, R'' = CH₂CH₃
- 6: R = R'' = H, R' = CH₂CH₃
- 7: R = CH₃, R' = R'' = H
- 8: R = CH₂CH₃, R' = R'' = H
- 9: R = CH₂OH, R' = R'' = H
- 10: R = R' = H, R'' = CH₂OH
- 11: R = CH₂OH, R' = H, R'' = CH₃
- 12: R = R' = H, R'' = CH₂CH₂OH

drates. However, previous to this work, there were no MM2 parameters for species containing the C—O=C linkage, present

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[§] Dedicated to Ernest Eliel on the occasion of his 70th birthday.

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(1) (a) The University of North Carolina. (b) Burroughs Wellcome. (2) (a) Goto, K.; Chitani, T. *Bull. Chem. Soc. Jpn.* 1941, 16, 403. (b) BeMiller, J. A. *Adv. Carbohydr. Chem.* 1967, 22, 25-108. (c) Bochkov, A. F.; Zaikov, G. E. *Chemistry of the O-Glycosidic Bond, Formation and Cleavage*; Pergamon: New York, 1979; pp 177-201. (3) Cordes, E. H. *Prog. Phys. Org. Chem.* 1969, 4, 1-44. (4) Edward, J. T. *Chem. Ind.* 1955, 1102-1104. (5) Toullec, J. J. *Chem. Soc., Perkin Trans. 2* 1989, 167-171.