to that of the other oxo–amino form (1) that is predicted to be the most stable in aqueous solution.

As far as tautomers 1, 2, and 4 are concerned, the PCM treatment results in *relative* electrostatic contributions to the solvation free energy that are similar to those from the SCRF method, giving an energy ordering in aqueous solution, 1 < 2 < 4. However, the solvation energies of 1 and 5 are now predicted to be very close, due to the same functional groups being present, rather than considerably different, as in the SCRF treatment, due to their considerably different dipole moments. Thus, in the SCRF treatment the relative energies are 1 < 5 < 2 < 4, while the PCM calculation gives 1 < 2 < 4 < 5.

Turning now to a comparison with experiment, temperature jump spectroscopy[2] shows that in aqueous solution, cytosine exists mainly as the 1(*H*)-amino–oxo form (1), in agreement with the prediction of both computational methods. However, experimentally, the other oxo–amino form (5) is found to be higher in energy than 1 by 15 kJ mol^{-1}, with the imine form (2) a further 9 kJ mol^{-1} higher in energy.[2] This experimental ordering, 1 < 5 < 2, clearly agrees well with the results of the SCRF model, while the PCM treatment is seen to give an incorrect ordering of the tautomers. We note that both methods predict values of the relative solvation free energies of tautomers 1 and 2 in excellent agreement with that obtained from the FEP method (17 kJ mol^{-1}).[13]

Conclusions

The ab initio calculations described here show that it is necessary to include polarization functions on all atoms to predict the correct relative energies of the tautomers of cytosine, with electron correlation and zero-point energies being relatively unimportant. It is found that geometry optimization at the 3-21G level is adequate. The inclusion of solvation effects by both SCRF and PCM models yields relative energies of tautomers 1 and 2 in excellent agreement with the experimental estimate. However, it is only the SCRF model that predicts the two oxo–amino tautomers to be close in energy in water, in agreement with experiment. This is somewhat surprising in view of the more accurate representation of the solute charge distribution which is expected to result from the PCM description.

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Registry No. Cytosine, 71-30-7.

Theoretical Structures of Methylenecyclopropane-2-carboxamide and Related Three-Membered Rings with Exocyclic Unsaturation. The Origin of a Ground-State Distortion

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Crystal structures of methylenecyclopropane-2-carboxamide reported by Van Derveer et al. and Schultz et al. show a distortion of the exocyclic methylene group such that it bends in the direction of the substituted ring carbon. Ab initio molecular orbital calculations were performed on a series of methylenecyclopropane derivatives, including methylenecyclopropane-2-carboxamide, as well as 2-formylcyclopropanone and 2-formylcyclopropanimines, in order to determine the origin of this ground-state distortion. Electron-withdrawing substituents cause a 3° to 4° distortion of the exocyclic methylene group toward the substituted ring carbon. Two electronic interactions, working alone or in tandem, are possible explanations for the distortion of the exocyclic methylene group. The first interaction proposed is between the π^* orbital of the substituent and a Walsh orbital of the three-membered ring, which causes a distortion of the three-membered ring. The distorted ring causes a distortion of the exocyclic methlene group. The second interaction proposed is between the π^* orbital of the substituent and the π orbital of methylenecyclopropane. The exocyclic methylene group distorts toward the substituent in order to increase the stabilizing interaction.

Introduction

Since the discovery that methylenecyclopropane (MCP) undergoes a degenerate thermal rearrangement,[1] MCP and its derivatives have been the focus of numerous experimental[2] and theoretical[3,4] studies. Recently, Van Derveer et al. reported the X-ray crystal structure of MCP-2-carboxamide, which showed distortion of the exocyclic methylene group toward the substituted ring carbon and the vinyl hydrogens tilted out of the plane of the carbon skeleton. These distortions are in the same direction as the motions which occur during the preferred rearrangement pathway.[5] Because of our interests in the effects of substituents on the stereochemical outcome of reactions and on ground-state distortions,[6] we undertook an ab initio

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Table I. Calculated and Experimental Structures of Methylenecyclopropane-2-carboxamide

			X-ray[5]		neutron diffraction[7]	
	3-21G	6-31G*	molecule 1	molecule 2	molecule 1	molecule 2
bond						
C_1–C_2 (R_1)	1.483	1.474	1.477	1.481	1.471	1.475
C_2–C_3 (R_2)	1.544	1.530	1.545	1.551	1.522	1.524
C_1–C_3 (R_3)	1.458	1.450	1.458	1.450	1.442	1.433
C_1–C_4	1.299	1.306	1.301	1.300	1.317	1.321
C_2–C_7	1.490	1.500	1.494	1.480	1.490	1.484
C_7–O_8	1.218	1.199	1.240	1.243	1.234	1.241
C_7–N_9	1.355	1.357	1.328	1.321	1.316	1.321
angle						
C_2–C_3–C_1	59.1	59.2	58.8	59.1	59.5	59.8
C_2–C_1–C_3	63.3	63.1	63.5	64.0	63.0	63.2
C_2–C_1–C_4 (A_1)	146.3	146.4	145.5	145.4	146.1	145.8
C_3–C_1–C_4 (A_2)	150.4	150.5	150.9	150.3	150.9	150.6
C_2–C_7–O_8	122.5	122.9	121.5	121.1	121.5	121.5
C_2–C_7–N_9	115.0	114.8	116.2	116.7	116.4	116.3
C_7–C_2–C_3	114.6	117.4	116.9	118.2	117.0	117.3
C_7–C_2–C_1	116.3	118.7	117.7	117.9	117.0	116.9
dihedral angle						
C_2–C_3–C_1–C_4	179.9	179.5	−178.6	−173.5	179.9	−172.8
C_3–C_2–C_1–C_4	−179.9	−179.6	178.8	174.3	−179.9	173.8
C_2–C_1–C_4–H_5	−0.7	−1.2	−1.9	−17.6	−0.7	4.8
C_2–C_1–C_4–H_6	179.8	179.3	−177.5	−174.8	179.8	−173.5
C_3–C_1–C_4–H_5	179.8	179.6	175.9	152.0	179.8	173.4
C_3–C_1–C_4–H_6	0.4	0.1	0.4	−5.2	0.4	−4.9
C_7–C_2–C_1–C_3	−103.6	−105.9	−105.8	−103.6	−103.6	105.8
C_7–C_2–C_3–C_1	106.6	108.2	107.2	106.6	106.6	−106.5
O_8–C_7–C_2–C_1	44.5	47.1	44.3	44.5	44.5	35.2

Table II. RHF/3-21G Geometric Parameters for Methylenecyclopropane and Various 2-Substituted Derivatives

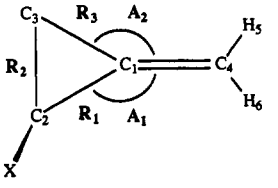
substituent	R_1	R_2	R_3	A_1	A_2	ΔA
NH_2	1.468	1.552	1.476	147.6	148.7	1.1
OH (anti)[a]	1.462	1.537	1.477	148.3	148.7	0.4
OH (syn)[a]	1.473	1.521	1.477	149.1	148.8	−0.3
OH (IN)[a]	1.467	1.531	1.486	149.3	148.1	−1.2
F	1.461	1.517	1.482	149.1	148.7	−0.4
CH_3	1.471	1.541	1.476	148.5	148.4	−0.1
H	1.472	1.545	1.472	148.4	148.4	0.0
CN	1.483	1.553	1.463	146.0	150.4	4.4
CO_2H (IN)	1.484	1.548	1.457	146.0	150.5	4.5
CO_2H (OUT)	1.482	1.550	1.457	146.0	150.3	4.3
CHO (IN)	1.488	1.548	1.456	146.0	150.5	4.5
CHO (OUT)	1.480	1.553	1.460	146.5	149.7	3.2
CHO (90°)	1.462	1.546	1.477	147.9	148.7	0.8
CHO (−90°)	1.467	1.543	1.475	147.8	148.9	1.1
$CONH_2$ (IN)	1.483	1.544	1.459	146.3	150.4	4.1
$CONH_2$ (OUT)	1.472	1.551	1.466	147.3	149.0	1.7
BH_2	1.498	1.582	1.451	145.8	149.4	3.6

[a] The OH conformations are defined as IN when the hydroxyl proton is oriented over the ring, syn when the hydroxyl proton is oriented away from the ring and toward the exocyclic methylene group, and anti when the hydroxyl proton is oriented away from the ring and away from the exocyclic methylene group.

molecular orbital study of substituted MCPs and related compounds. One point of interest is whether the distortions of MCP-2-carboxamide, some of which are only present in one of the two nonequivalent molecules in the unit cell,[5,7] are inherent molecular properties or are due to crystal packing forces. During the course of our work, Schultz et al. reported a neutron diffraction crystal structure of MCP-2-carboxamide.[7] The same distortion of the exocyclic methylene group toward the substituted ring carbon was observed, but the vinyl hydrogens were found to be in the plane of the ring. As shown below, ab initio calculations give excellent structural predictions and also permit an interpretation of the observed structural distortions.

Results and Discussion

The geometry of MCP-2-carboxamide was optimized with the 3-21G[8] and 6-31G*[9] basis sets using Pople's GAUSSIAN 88 program.[10] The geometric parameters obtained from these calculations, along with those from the X-ray and neutron diffraction crystal structures, are presented in Table I. There is good agreement between the ab initio structures and molecule 1 of both crystal structures, including the distortion of the exocyclic methylene group toward the substituted ring carbon. The RHF/6-31G* bond lengths are within ±0.04 Å of those for molecule 1 and 2 for both crystal structures. The calculated angles are within ±1° of the experimental values for most angles, including the angles describing the distortion of the exocyclic methylene group, C_2–C_1–C_4 (A_1) and C_3–C_1–C_4 (A_2). These angles are calculated to be 146.4°



(A_1) and 150.5° (A_2) with the 6-31G* basis set, while experimentally these angles are found to be 145.5–146.1° (A_1) and 150.3–150.9° (A_2). Since the calculations on the isolated molecule accurately reproduce the distortion of the exocyclic methylene group toward the substituted ring carbon, this distortion is the result of the carboxamide

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Table III. Total Energies of the Carbonyl Substituted MCPs for the IN and the OUT Conformations As Calculated at the RHF/3-21G Level of Theory. The Relative Energies Are Given in Parentheses. The Total Energies Are Given in Hartrees. The Relative Energies Are Given in kcal/mol

substituent	IN	OUT
CHO	−266.107 49 (0.2)	−266.107 77 (0.0)
CO_2H	−340.586 74 (0.0)	−340.586 06 (0.4)
$CONH_2$	−320.868 79 (0.0)	−320.866 58 (1.4)

substituent, not crystal packing forces. In molecule 2 of both crystal structures, the exocyclic methylene group is also distorted out of the plane of the ring by 6–8° (see dihedral angles C_2–C_3–C_1–C_4 and C_3–C_2–C_1–C_4 in Table I). This distortion is not reproduced by the calculations and is not present in molecule 1 of either crystal structure. This distortion is most likely the result of crystal packing forces. While the RHF/6-31G* structure is in better accord with both crystal structures, the 3-21G basis set provides satisfactory trends in lengths and angles with a substantial savings of computer time. All structures subsequently discussed have been optimized using the 3-21G basis set.

In order to find an explanation for the distortion of the exocyclic methylene group toward the substituted ring carbon in MCP-2-carboxamide, a variety of substituents was studied, ranging from strongly electron-donating (–NH_2) to strongly electron-withdrawing (–BH_2). The degree of the distortion is determined by the difference (ΔA) between two angles, A_2–A_1. A positive value for ΔA indicates that the distortion is in the direction of the substituted ring carbon, as in the carboxamide described above. The results are given in Table II. When the substituent is electron-withdrawing, ΔA ranges from 3° to 4°. No obvious trend can be found for ΔA when the substituent is electron-donating.

One hypothesis proposed to explain these results involves the interaction between one of the occupied Walsh orbitals of the cyclopropane ring and the π^* orbital of the electron-withdrawing substituent. This interaction is shown in Figure 1. This type of conjugation between a substituent and a cyclopropane ring was invoked by Hoffmann to explain the influence of substituents on the equilibra between cycloheptatrienes and norcaradienes.[11a]

Electron-withdrawing substituents, such as esters and cyano groups, cause the equilibrium to be shifted in favor of the norcaradienes. Hoffmann proposed that a vacant π^* orbital of the substituent interacts with a filled Walsh orbital, as in Figure 1; this interaction causes a transfer of electron density from the ring to the substituent, causing a decrease in the antibonding character of R_3 and a decrease in the bonding character of R_1 and R_2. This results in a decrease of the bond length of R_3, and an increase of the bond lengths of R_1 and R_2. The strengthening of R_3 shifts the equilibrium toward the side of the norcaradienes.[11] Allen et al. examined a large number of crystal structures of substituted cyclopropanes and found that in cases where the substituent is electron-withdrawing, the distal bond (R_3) is shortened and the vicinal ring bonds (R_1, R_2) are lengthened relative to cyclopropane.[12]

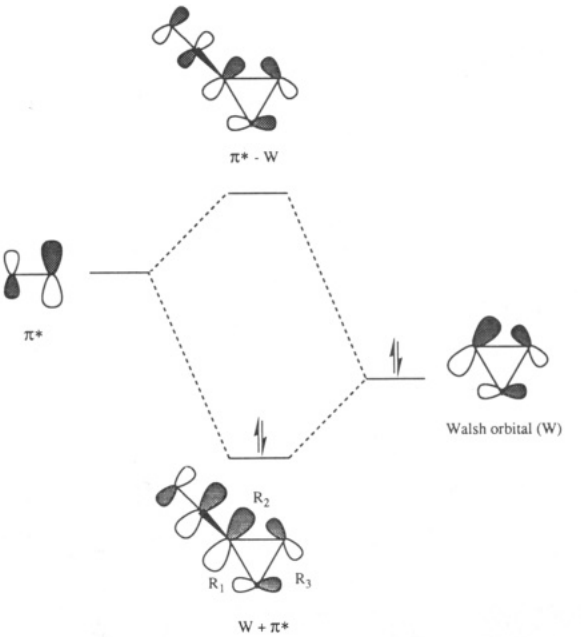

Figure 1. Diagram showing the interaction between the π^* orbital of a substituent and a Walsh orbital (W) of a three-membered ring.

The same trend is found in the calculated structures of substituted MCPs. The bond lengths of the ring bonds for all MCP derivatives calculated are listed in Table II. Good π-acceptors, like CHO, cause R_1 and R_2 to lengthen and R_3 to contract. A methyl group, which is a very weak π donor, has a very small effect, and even the better donors, F, OH, and NH_2, cause relatively small increases in R_2 and R_3 and a small decrease in R_3. The net result of these bond length changes are that all acceptors generally cause a 3°–4° difference between A_1 and A_2, while donors cause changes of only ±1°. This distortion of the three-membered ring is proposed to cause a decrease in A_1 and an increase in A_2.

For each carbonyl derivative, there are two conformations of the substituent that are minima with respect to rotation about the $C_{substituent}$–C_{ring} bond. These conformations are defined as IN and OUT, where IN indicates that the carbonyl oxygen is oriented over the ring and OUT indicates that the carbonyl oxygen is oriented away from the ring. The geometries of both conformations of 2-formyl-MCP are shown in Figure 2. The crystal structure of MCP-2-carboxamide is found to be in the IN conformation. The IN conformation is calculated to be 1.4 kcal/mol more stable than the OUT conformation at the RHF/3-21G level. The OUT conformation of 2-formyl-MCP is favored by 0.2 kcal/mol, while the IN conformation of 2-carboxyl-MCP is favored by 0.4 kcal/mol.

In order to show that conjugation is responsible for the ring distortion, which in turn causes the distortion of the exocyclic methylene group, the structures of 2-formyl-MCP with the formyl group rotated 90° or −90° from the IN conformation were optimized (Figure 2). Elimination of conjugation between the carbonyl π^* orbital and the cyclopropane Walsh orbital should cause the distortion of the three-membered ring to be greatly diminished, which should cause ΔA to decrease. In both the 90° and −90° conformers (Table II), the distortion of the three-membered ring and the exocyclic methylene group decrease. ΔA is 1.2° for the 90° structure and 0.8° for the −90°

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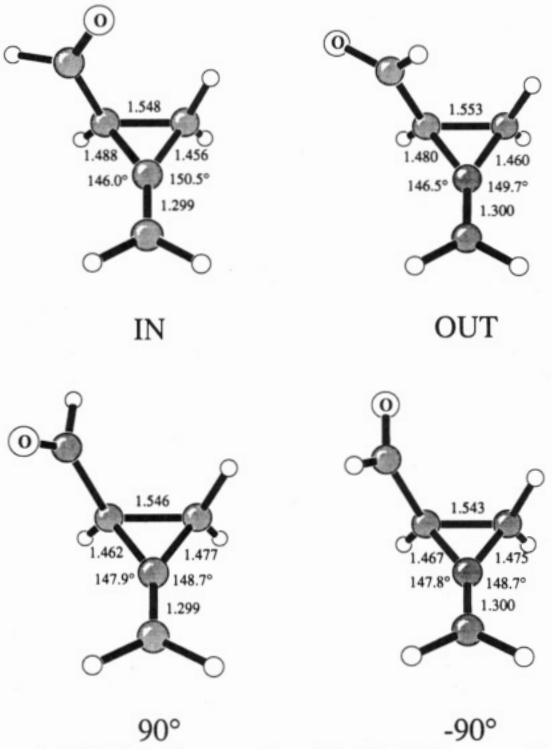

Figure 2. RHF/3-21G geometries of the IN, OUT, 90°, and −90° conformations of 2-formyl-MCP.

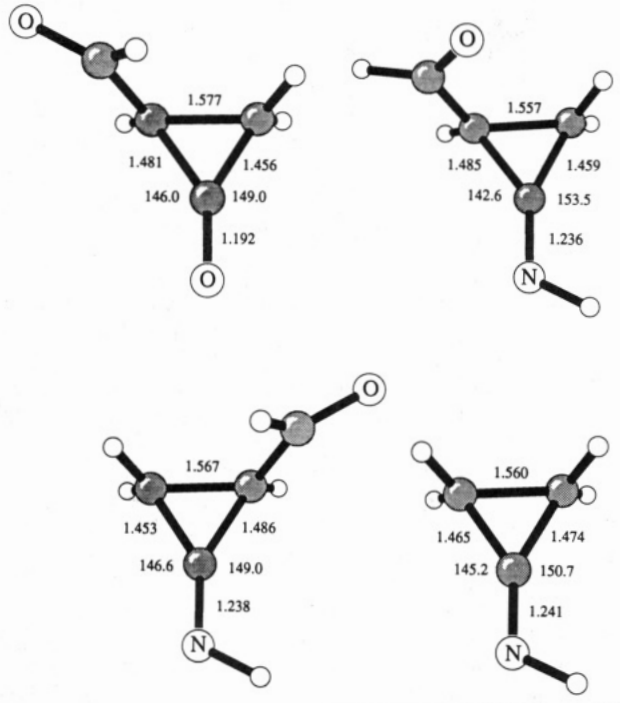

Figure 3. RHF/3-21G geometries of 2-formyl-CPO, *anti*-2-formyl-CPI, *syn*-2-formyl-CPI, and CPI.

structure versus 4.5° for the IN conformation and 3.2° for the OUT conformation.

The same type of distortions found in the substituted MCPs is expected to occur in appropriately substituted cyclopropanones (CPO) and cyclopropanimines (CPI). The geometries of 2-formyl-CPO and *anti*-2-formyl-CPI were optimized and are shown in Figure 3. The ΔA for distortion of the exocyclic oxygen is 3.0° while the ΔA for the exocyclic nitrogen is 9.7°. As expected, a CPO and CPI with an electron-withdrawing substituent undergo the same distortion of the exocyclic group as the MCP derivatives. While the distortion of the 2-formyl-CPO is of the same magnitude as 2-formyl-MCP, the ΔA for *anti*-2-formyl-CPI is significantly larger. The cause of this additional distortion is the result of a repulsive 1,4-interaction between the exocyclic proton and the unsubstituted ring carbon. The repulsive 1,4-interaction is also present in *syn*-2-formyl-CPI and CPI. The ΔA for CPI is 5.5°; ΔA for MCP and CPO is 0°. When an electron-withdrawing substituent is added to CPI, the distortion caused by the substituent reinforces the 1,4-repulsion in *anti*-2-formyl-CPI; ΔA is increased by 5.2°. These two effects cancel in *syn*-2-formyl-CPI; now ΔA is −2.4°, 3.1° less than ΔA in CPI.

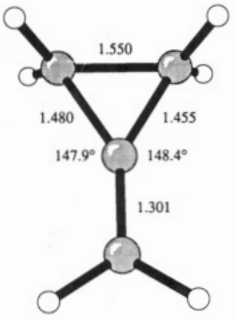

Figure 4. RHF/3-21G structure of distorted MCP with the ring CC bonds held constant.

As a final test of the distorted ring hypothesis, we optimized the structure of MCP with the ring CC bond lengths fixed to values comparable to the substituted MCPs (R_1 = 1.455, R_2 = 1.480, R_3 = 1.550). The structure is shown in Figure 4. There is a distortion of the exocyclic methylene group (ΔA = 0.5), though of a smaller magnitude than found in the substituted MCPs. The distortion of the cyclopropane ring by electron-withdrawing substituents does distort the exocyclic methylene group, although it may not be the only effect responsible for the latter distortion.

Another possibility is an interaction of the π^* orbital of the substituent with the exocyclic π system. This interaction involves overlap of the p orbital on the carbon of the substituent with the lobe on the exocyclic carbon. The ground-state conformations of the substituted MCPs situate the lobe on the substituent carbon in the best position to interact with the exocyclic carbon p orbital, causing the largest distortion of the exocyclic methylene group (ΔA). When the substituent is rotated ±90°, the p orbital on the substituent carbon interacts less with the exocyclic methylene p orbital, decreasing the distortion of the exocyclic methylene group. This is observed for the ±90° rotated 2-formyl-MCPs (Figure 3).

Conclusion

Although a quantitative dissection of the origins of this distortion has not been achieved, the dependence of the magnitude of the distortion on the type and orientation of the substituents has been established, and calculations with the 6-31G* basis set have been shown to be in excellent agreement with experiment.

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Supplementary Material Available: Archive entries of the ab initio calculations described in this paper (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.